

MEDICINE

HANDWRITTEN NOTE

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Name : _____

Subject : _____ **Medicine**



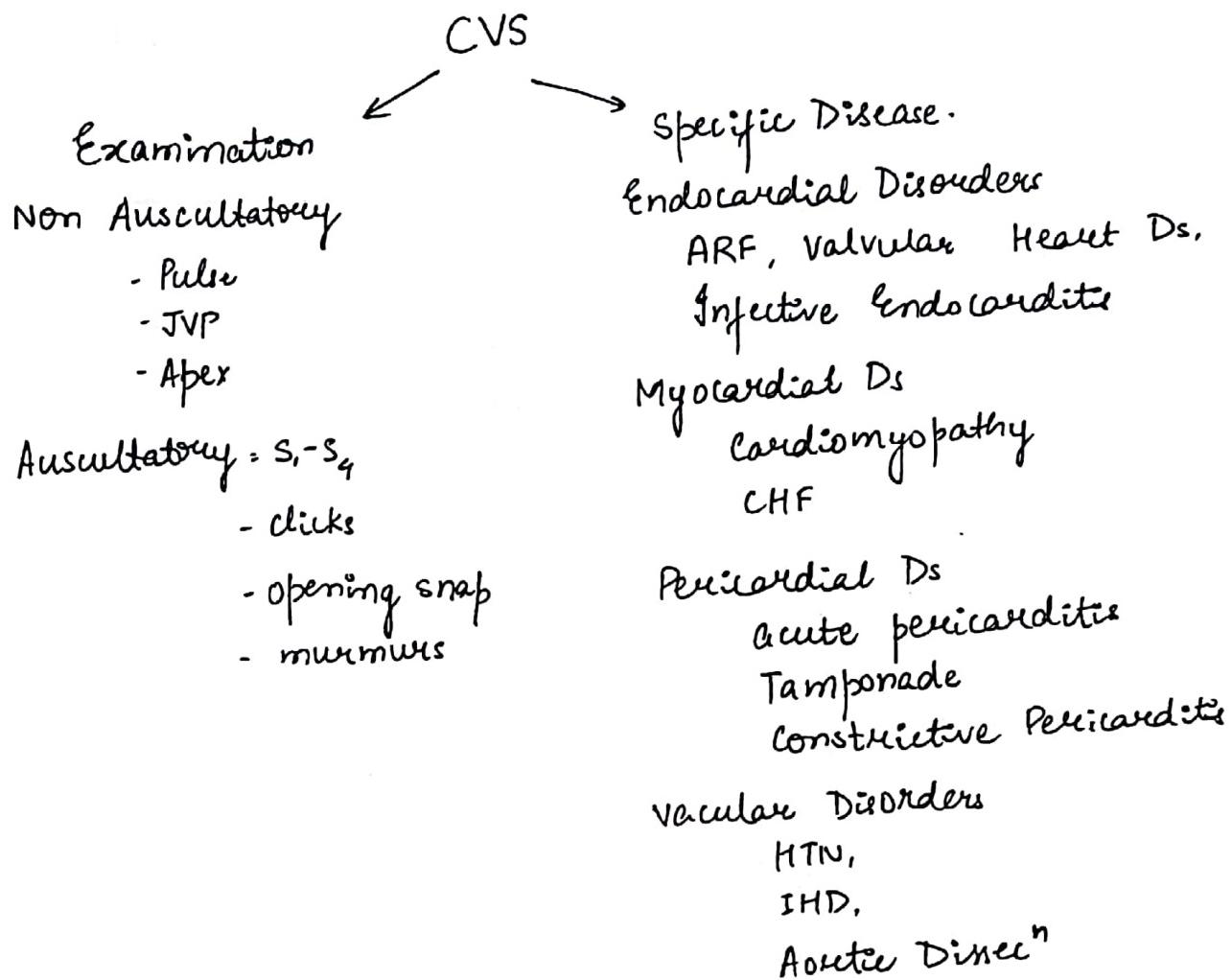
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CVS

RHEUMATOLOGY

RESPIRATORY

ACID - BASE BALANCE



PULSE

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(I) Pulse Rate

(N) 60 - 100/min

Ab (N)

1) **Bradycardia** - < 60/min.

Causes

Physiological

- 1) Elderly
(age related SA node degeneration)
- 2) Sleep
(↓ in sympathetic activity)
- 3) Athletes
(Basal ↑ in vagal D/c)

Pathological

I) **CVS Cause**

- 1a) Brady arrhythmias
(AV Block)
- 2) MI [inf. wall]
SA node → due to stimulation
also supplied by vagal n/v nearby
② coronary artery

II) **Non-CVS Causes**

- 1) Hypothyroidism
- 2) Hypothermia
(directly affects SA Node)

3) Drugs

- a) β blocker
- b) non DHP CCB [cause AV Block]

c) ~~Digoxin~~ Digoxin. effect

4) ↑ ICP

Cushing's reflex = BP↑, HR↑, irregular resp

To perfuse brain systemic
BP↑ → stimulate baro
receptors in carotid
release vagal D/c

↑ Bile \Rightarrow SA node

⑤ Obstructive jaundice

2) Tachycardia $> 100/\text{min}$

CAUSES

Physiological

1) Infants (\uparrow SA node activity)

2) Anxiety
(\uparrow sympathetic activity)

3) Exercise
(\uparrow demand)

Sympathetic system \leftarrow Thoracic n/s
[Thoracolumbar]

Pathological

① CVS causes

1) Tachyarrhythmias, arrhythmias.

a) PSVT

b) AF

2) MI (ant. wall)

[Stimulation of nearby sympathetic n/s]

② Non-CVS causes.

1) Hyperthyroidism.

2) Fever.

3) Bébi - Bébi

4) Drugs

a) β agonist

b) short acting DHPs [reflex tachycardia due to compensation]

c) Digoxin toxicity

d) Theophyllin

e) Thyroxin.

③ Relative Bradycardia / Faget's Sign Q,

HR doesn't ↑ in proportion to body temperature.

(N) For every 1°C from 37°C .

\downarrow
HR ↑ by $15-20/\text{min}$ from baseline

For every 1°F from QBF \rightarrow HR ↑ by $10/\text{min}$.

e.g. if Body Temp is 40°C . $\text{HR} = 112/\text{min}$ (baseline = $80/\text{min}$)
 min expected $\text{HR} = 80 + 45$
 $= 125$.

Causes

Infectious

(also ⊕ SA node)

- 1) Typhoid fever
- 2) Brucella
- 3) Legionella
(sputum AFB +ve)
- 4) Viral

Non-Infectious

- 1) Drug induced fever
- 2) Self induced fever or Factitious Fever. Q.
- 3) Fraudulent Fever
(thermometer only).

(II) Rhythm :-

(N) → Regular = Fixed interval b/w any 2 consecutive pulses



Ab (N)

Physiological

Sinus arrhythmia

HR changes in inspiration & expiration

Pathological.

During Inspiratory Phase

-ve Intrathoracic Pressure

↑ Blood flow into (R) side of heart

Pulmonary vessels dilatation
(blood pooling)

↓ blood flow into (L) side of heart

CO will ↓

SBP will ↓

Baoroceptor stimulation ↓

Vagal release ↑

HR ~~↓~~ ↑

During Expiratory Phase.

(+) Intrathoracic Pressure

↓
↓ blood flow into R side of heart
↓

Pulmonary vessels are squeezed
↓

↑ blood flow into L side of heart

CO will ↑

[SBP ↑]

Baroreceptor (+)↑

Vagal ↑

[HR ↓]

Pathological

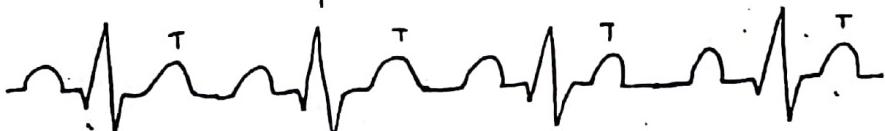
I) Regularly irregular rhythm

↓
predictable ↓
variable.

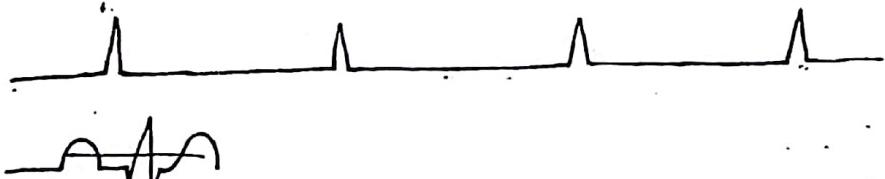
CAUSE :- 1) [Bigeminy Rhythm] ← Digoxin Toxicity

every alternate ventricle contract & depolarize
is due to premature ventricular ectopic

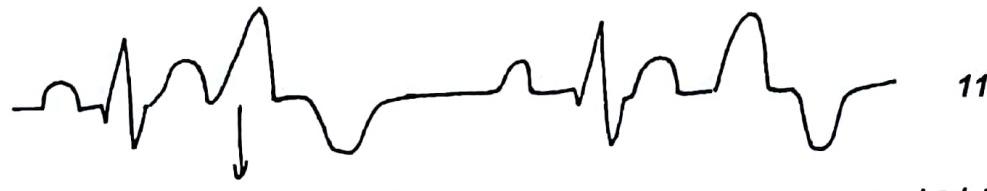
(N) ECG.



Pulse



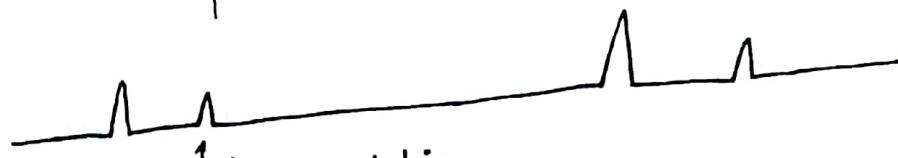
Bigemny



premature ventricular ectopic [wide p. QRS prolonged, inverted T.
due to abnormal depolarization]

Pulse

Bigeminus



↓ due to ectopic.

↓ amplitude due to ↓ ventricle filling time
hence ↑ stroke volume

II Irregularly Irregular Rhythm

↓ no predictable variation in interval.

CAUSE = Atrial fibrillation. = variable HR

III PULSE PRESSURE.

How well a. felt

$$\textcircled{N} = \text{SBP} - \text{DBP} [30-60 \text{ mm Hg}]$$

Ab \textcircled{N}

I) ↓ PP. / Threadbare Pulse.

Mech. if $\boxed{\text{SBP } \downarrow}$ & $\boxed{\text{DBP } \uparrow}$

↓
if CO ↓

Stimulate sympathetic activity

↓
arteriolar constricⁿ



PVR ↑

CAUSE = Shock [Hypovolemic, shock]. 12
not found in septic or neurogenic shock.

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II> ↑ PP / Bounding Pulse.

Mech - if SBP ↑ or DBP ↓
 occurs if COT
 to ↓ LV st Main → PVR ↓

CO is inversely related to PVR

CAUSE : 1) ↑ CO state

- 1) AR
- 2) MR.
- 3) PDA

Physiological → ♀
when plasma vol r.

Pathological →

1) Hyperthyroidism

β , rec +

ionotropic

chronotropic

$$\text{COT} = \text{TSV} \quad x$$

HRT

(N) vit B₁, ⊖ NO synthase

2) Anaemia

3) $B_{\text{eff}} - B_{\text{ext}}$

if Def of VGB,
↳ vaso dilatation

↓ PYR ↓ → COT↑

PVR ↓ as
arteriole are
bypassed
↳ CO↑

- 4) A-V fistula
- 5) Paget's Disease
[A-V fistula in Bone]

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Q. \subseteq [low CO state] will cause [bounding Pulse]?

Ans. severe bradycardia \subseteq [complete AV Block]

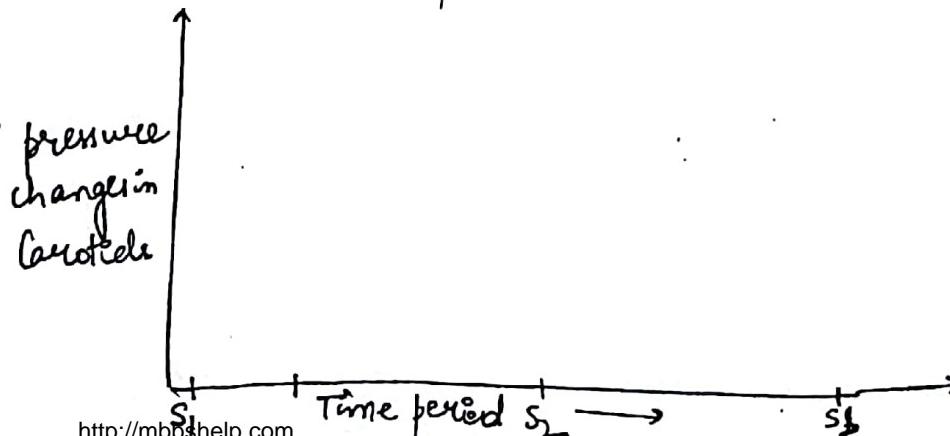
$$SV \uparrow \times HR \downarrow \rightarrow CO \downarrow$$

AV Block \rightarrow ↓ depolarization of ~~pacemaker~~ Purkinje fibers
 \downarrow
 Rate \downarrow [firing speed is less in AVN]
 \uparrow
 But EDV ↑
 \uparrow
 SV ↑

(W) CHARACTER

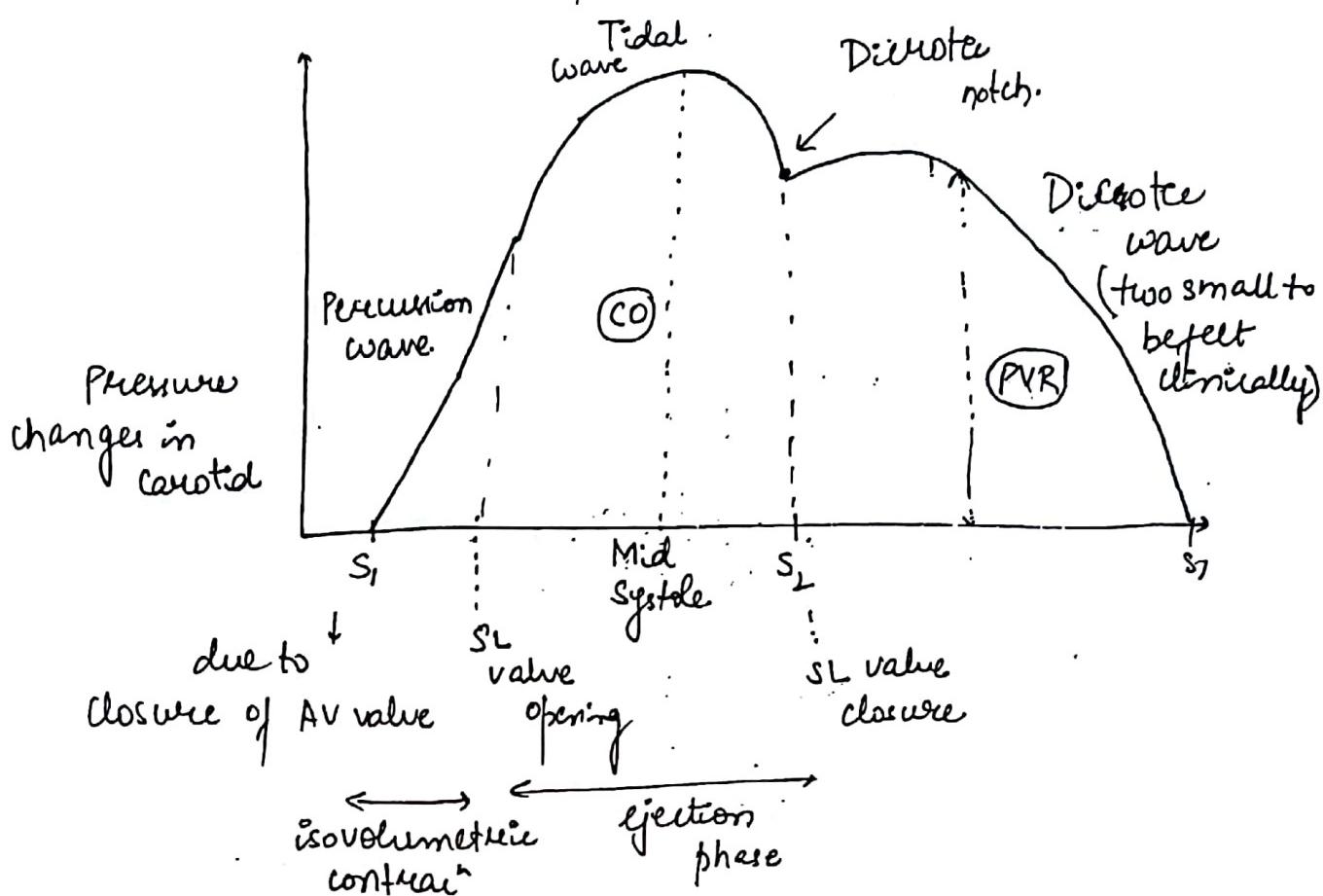
Rate	Rhythm	best assessed in	Radial artery
character / contour	"	"	Carotid artery

(N) Waveforms of carotid.



S_1 is due to closure of AV valves

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WAVE

① Perfusion wave

MECH
It is due to pressure transmission by isovolumetric LV contraction onto carotid.

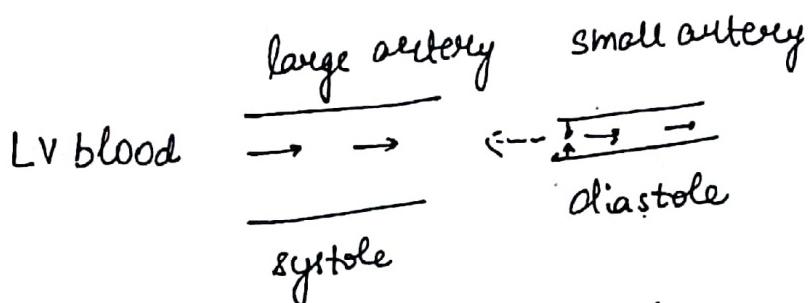
② Tidal wave

Below of blood ejected into carotid ring its pressure further.

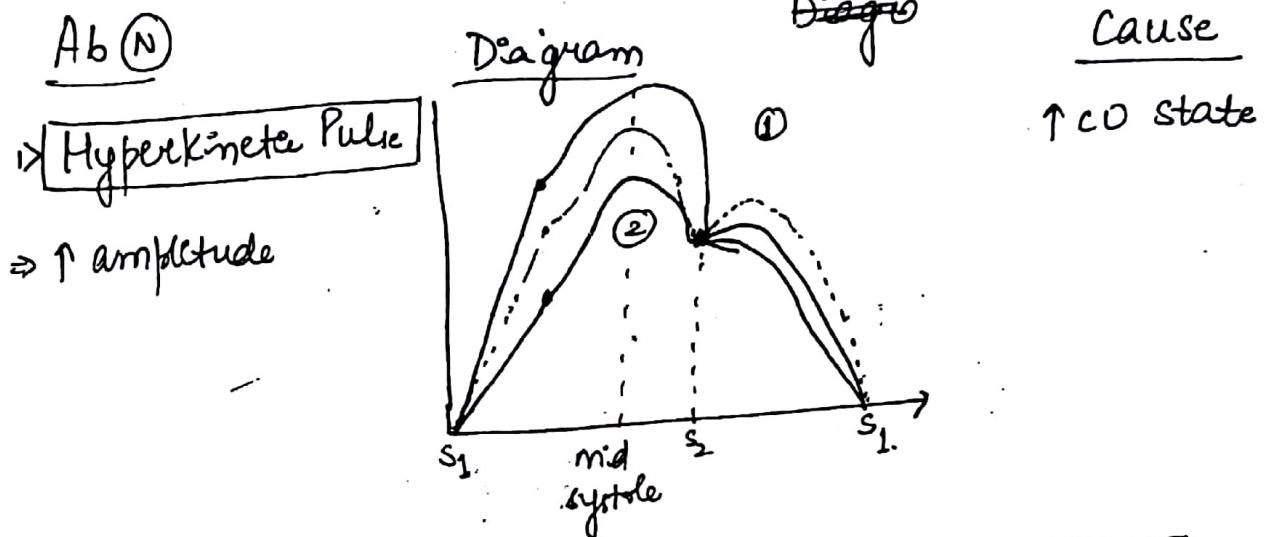
③ Dicrotic wave

Due to back pressure reflection from small vessels

Dicrotic notch represents closure of aortic + pulmonary valve (S_2)



Recoil of small vessel lead to the pressure impulse

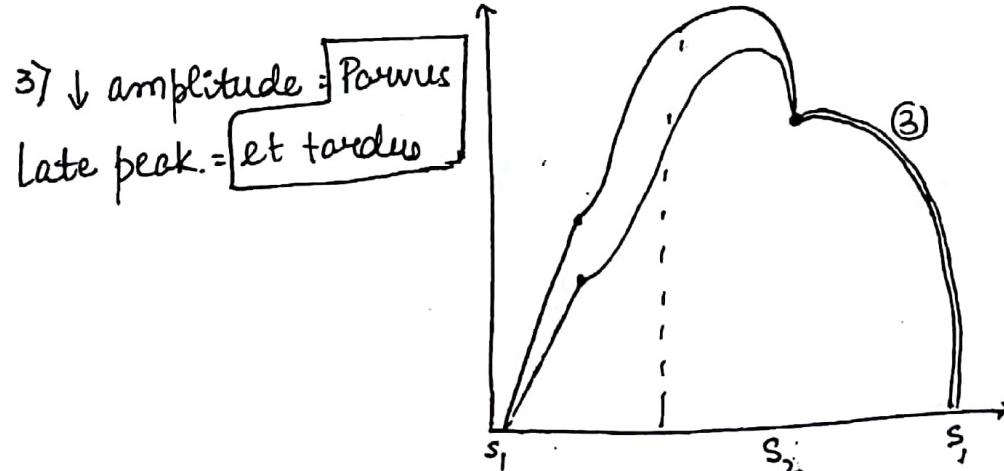


2) **Hypokinetic Pulse**
⇒ ↓ amplitude

though diastole wave
is ① but still not felt
not felt clinically.

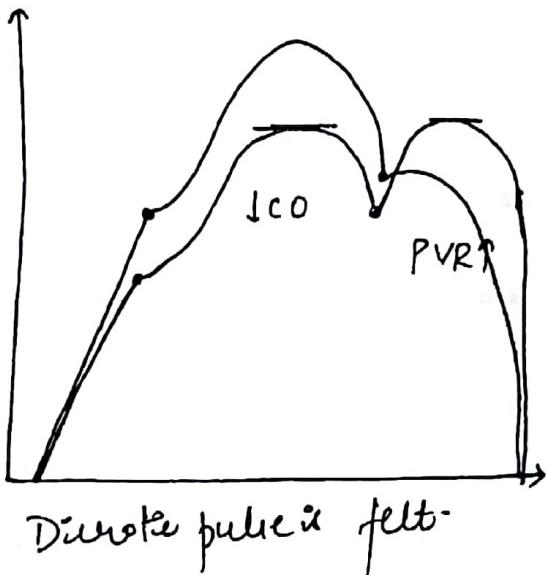
↑ CO state

most specific pulse of
severe AS.



④ **Dicrotic Pulse**

= 2 peaks
one in Systole
other in diastole

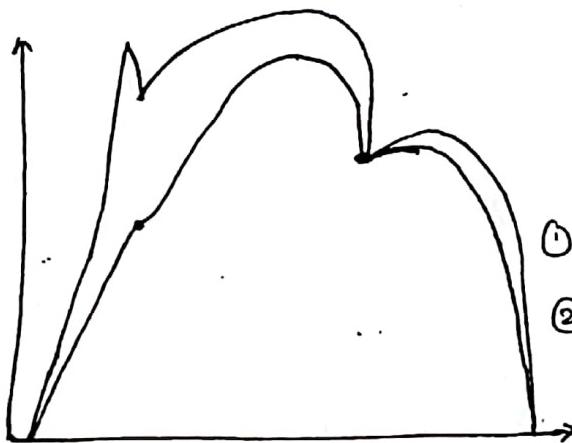


shock

(Hypovolemic
cardiogenic)

⑤ **Bifurcations Pulse**

= 2 peaks
① in Systole
Best assessed in
peripheral artery



Most specific pulse
of

- ① Severe AR.
- ② Severe AR + AS

Brisk isovolumetric ventricular contraction

(↑ LV vol. + ↑ stretching)

↓
Perfusion wave will shift to (as duration is less)

gets separated from tidal wave.

③ HOCM --- ?

If will make tidal wave to come late.

V MISCELLANEOUS POINTS IN PULSE.

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1) PULSUS ALTERNANS - Best assessed in Radial.

Regular alteration of pulse amplitude.



only amplitude changes, interval remain same

most specific pulse.

CAUSE → **LV (Systolic) Dysfunction**

2) PULSE DEFICIT :-

(N) HR - PR ← due to adequate SV = 0
↳ arterial pulsation is felt
due to ventricle contract

Ab (N) if $HR - PR = +ve \Rightarrow$ Pulse Deficit.

CAUSES

1) **AF c variable heart rate**

Pulse ↑
adequate ventricle filling
Here 5 HR but 3 PR

2) **Premature Ventricle Ectopics**

less filling time → pulse not felt

If pulse deficit $> +10/\text{min} \Rightarrow \text{AF only}$

3) PULSUS PARADOXUSES :-

(N) $\text{SBP}_{\text{exp}} - \text{SBP}_{\text{insp}} = 0 \text{ to } 10 \text{ mm Hg.}$

If this difference is $> +10 \Rightarrow$ ~~Pulse~~ Pulsus Paradoxus.

Exaggeration of Normal Phenomenon. hence paradoxical word is wrong.

Mech \downarrow in SBP_{insp} more than physio limits.

CAUSES

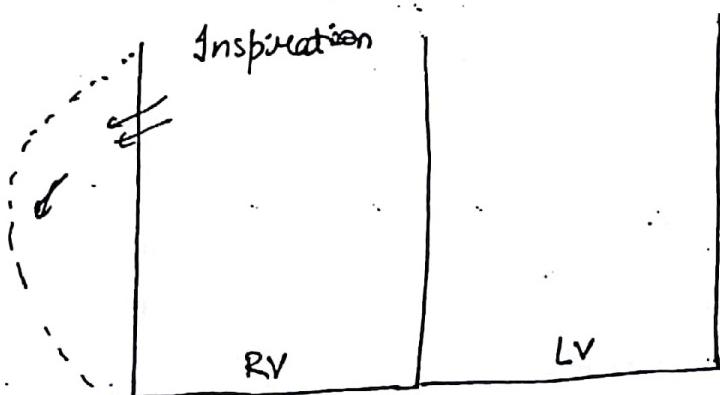
(I) CVS :- H/o CVS cause \Rightarrow **Cardiac Tamponade.**

"Compression" of heart due to pericardial effusion.

(N) During Inspiration,

Blood flow is more in **R** Ventricle

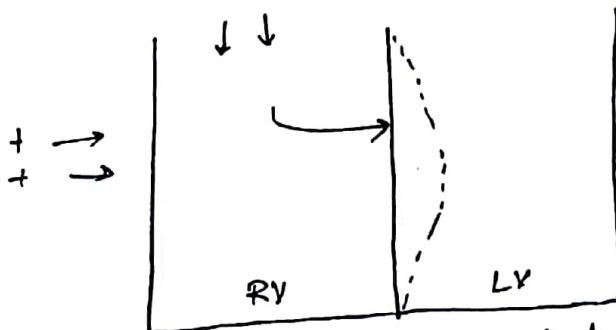
RV wall dilates to accommodate extra blood.



In Tamponade:

Inspiration
blood.

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RV wall can't dilate due to ~~pleural~~ pericardial fluid.

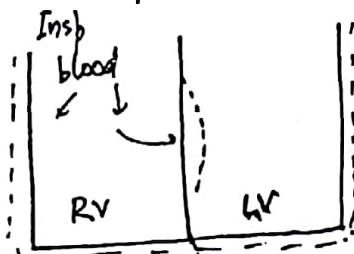
→ Septal bulge in LV → ↓ LV filling further

↓
CO ↓

↓
SPP ↓ during inspiration.
than physiological limits.

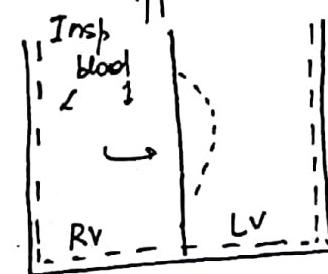
2) Constrictive Pericarditis

Failure of relaxation of heart due to stiff pericardium



3) Restrictive Cardiomyopathy

Failure of relaxation of heart due to stiff endomyocardium.



Septum should be spared from stiffness to cause this sign

II) Non CVS Cause

H/c overall cause →

Acute exacerbation of asthma or COPD.

2) Pulmonary embolism

3) Kussmaul breathing [due to met-acidosis]

4) Obesity

Q. 5) SVC Obstruction [reason not known].

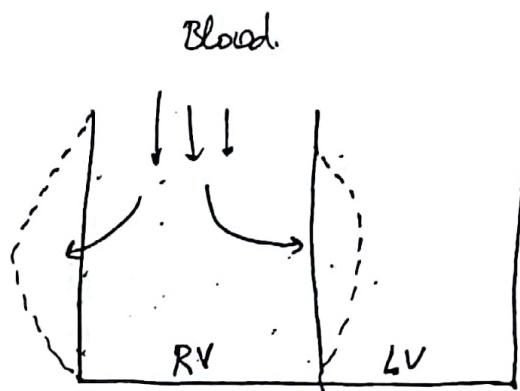
Deep Inspiratory efforts.

Large -ve intrathoracic pressure

↑↑↑ venous return to the right side

↓
Septal bulge.

Pulm Paradoxus



Due to extra blood
septal bulge occurs.



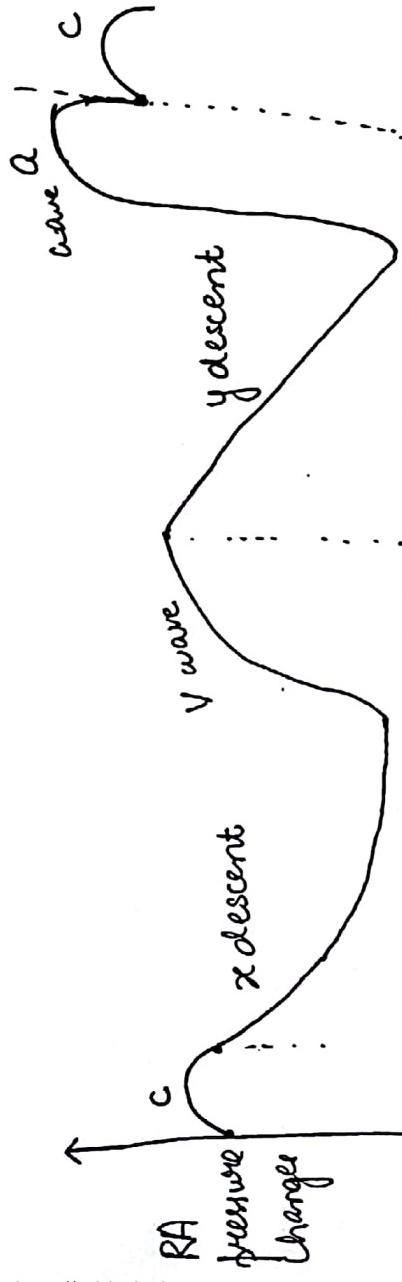
(N) measure of (R) atrial pressure seen in (P) IJV

(N) Height → [0-3cm from sternal angle]

} 5cm below

RA activity.

= [5-8cm from RV activity.]



$Q \subseteq$ wave \cup (B) right + diastole

\Rightarrow V wave

Q. E wave will be more
pronounced?

⇒ a game.

Q. Can different wells be more prominent?

$\Rightarrow x$ ~~was~~ descent

The diagram illustrates the sequence of events in the cardiac cycle:

- Opening of valves:** Indicated by arrows pointing towards the chambers.
- Closing of valves:** Indicated by arrows pointing away from the chambers.
- Phases:**
 - isovolumetric contraction:** Between atrial contraction and ventricular contraction.
 - ejection phase:** Between ventricular contraction and ventricular relaxation.
 - isovolumetric relaxation:** Between ventricular relaxation and atrial contraction.

Active RA
“contractor”

Picture R
"centre"

Passive blood
flow from
RA to RV

Venous
filling of
RA via
 $\text{SVC} + \text{IVC}$

“Reunited
values
pulled down
by RV centre”.

TV bulge into RA. Tricuspid valve (↑ RA pressure) shifted due

↑ RA pressure ↓ RA pressure

↑ RA volume

↑ RA pressure.

Ab(N) JVP

(I) **a wave** = due to (R) atrial contract

1) **Absent a wave** = if ineffective atrial contract

↓
AF

2) **Large a wave** = if (R) atria contracting against
Diastolic Wave more resistance

If (R) atria is contracting → Tricuspid valve gives resistance
 1) Tricuspid valve gives resistance
 2) RV also gives resistance

cause-

a) **Tricuspid stenosis**

b) RV pressure ↑

RVH
(concentric)
↑
due to (PS)

PAH

↓
RV failure
(systole)

RV blood retention.

"Compression of RV"

↓
Cardiac Tamponade

1) **Pulmonary embolism**
2) **RV MI**

3)

3) **Canon a wave** = if RA contracting against closed T. valve.
Systolic event → cause TV closure
occur if RA & RV are contracting simultaneously

causes → ① **Junctional rhythm.**
SA node arrest → AV node becomes pacemaker + impulse. Reach. (B) atria & ventricle simultaneously

Rate of Cannon a wave = 50/min, **regular**

② **Complete AV Block**

SA node will depolarise atria.
Purkinje fibres will depolarise ventricles independently

so occasionally atria & ventricle can depolarise simultaneously

Canon a wave is = **intermittent**

II **X Descent**

N due to tricuspid ring pulled down by RV contract during ejection phase.

R atria is free of significant blood (during this phase)

Ab N

1) Absent X Descent

if R atrial pressure doesn't fall as it contains

b ↓ I ↓ or ↓
significant Blood or Clot

significant blood
↑
(TR)

clot
↑
(AF)

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② Deep & Descent

occur if tricuspid ring pulled more downward due to

⇒ Increased RV contractility

③ 1) Cardiac tamponade

2) Constrictive Pericarditis.

III

V Wave

N due to venous filling of R atria

Ab(N)

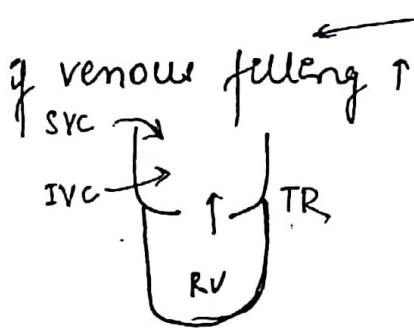
1) Absent or Low V wave :-

occur if venous filling of RA ↓

Cause - 1) obstructive SVC

2) Large V wave :-

If RA pressure ↑ during venous filling



if venous filling ↑ or ↓ compliance of R atria
[failure of relaxation]

- 1) constrictive pericarditis
- 2) Restrictive cardiomyopathy

(IV)

Y Descent

(N) due to passive blood flow from (R) atria to (R) ventricle ab(N)

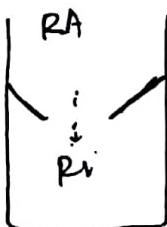
1) **Rapid Y Descent** :- / FREIDRICH'S SIGN.
will occur if (R) atrial blood moves very fast into (R) ventricle as soon as Tricuspid valve opens.

All causes
of large v = Rapid y

2) **Slow y Descent** :-

If (R) atrial blood moves into (R) ventricle slowly.

cause - 1) Tricuspid stenosis
2) ↑ RV pressure



Causes of Large a = Slow y

y descent absent - if RA blood doesn't move into RV during passive filling phase



occurs if (R) ventricle is fully "compremed."

Cardiac Tamponade.

Signs of JVP

① Abdomino Jugular reflex
[abdomen compressed for 10 sec]

Description

if JVP remain elevated by [more than 3cm] even after release of compression for >15 sec

Causes

Latent RVF ·
no RVF in basal state + RVF is manifested if RV workload ↑

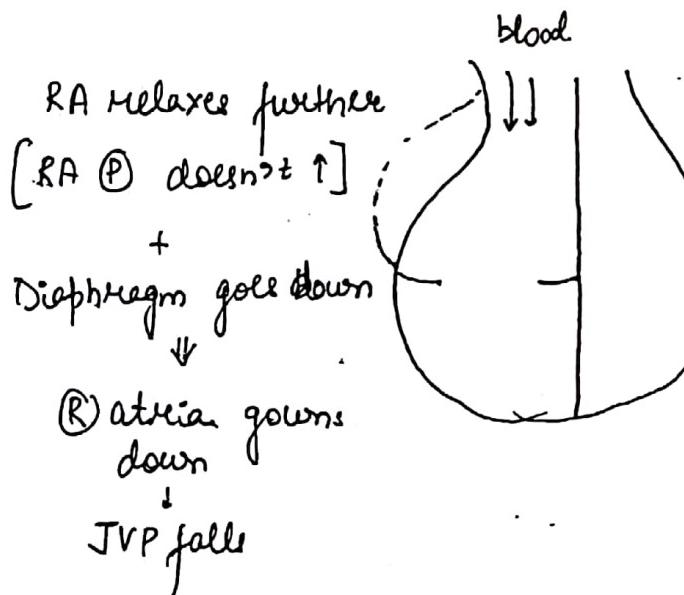
② Kussmaul's sign

↑ in JVP during inspiratory phase

(N) JVP ↓ during inspiration

if (R) atria fail to relax (N)

Constrictive pericarditis
Restrictive cardiomyopathy

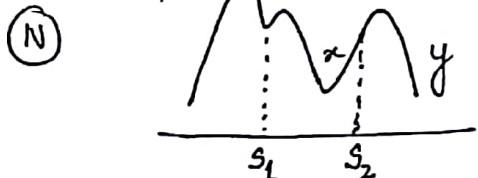


If basal RA P = TS RVF

Basal atrial 'P' ↑ due to
if AV valve Stenosis → ventricle failure

Kussmaul's Sign is absent in tamponade. - - - ?

Q. Δ of etiology :-



Ab(N)

①



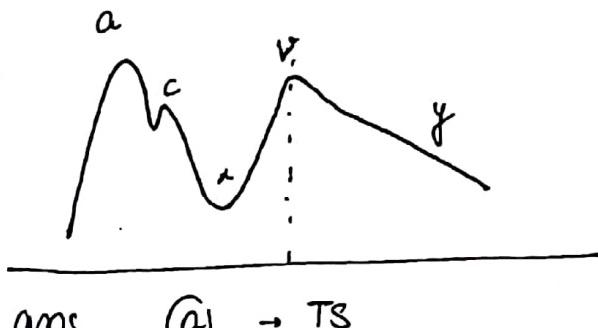
a) TS

b) constrictive
Pericarditis

c) Tamponade d) TR.

y is absent

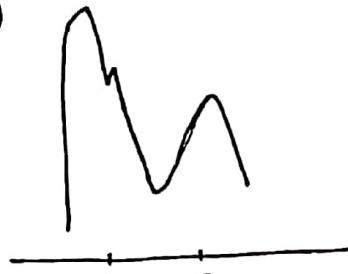
②



ans ② → TS

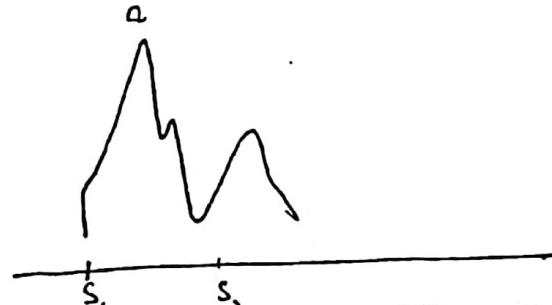
show y descent

③



①

Δ = large a
TS



②

Here a is systole
 \downarrow

Options

① TS

② Junctional
Rhythm

Δ = canon aware

\downarrow
Junctional Rhythm

APEX BEAT

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(N) due to iso volumetric contraction (D) ventricular contract.



LV apex displaced superiorly

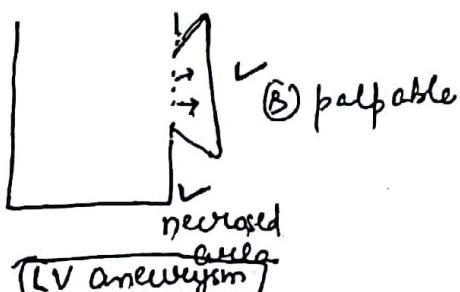
Nature → Tapping.

Site → (L) 5th ICS, just medial to mid-clavicular line

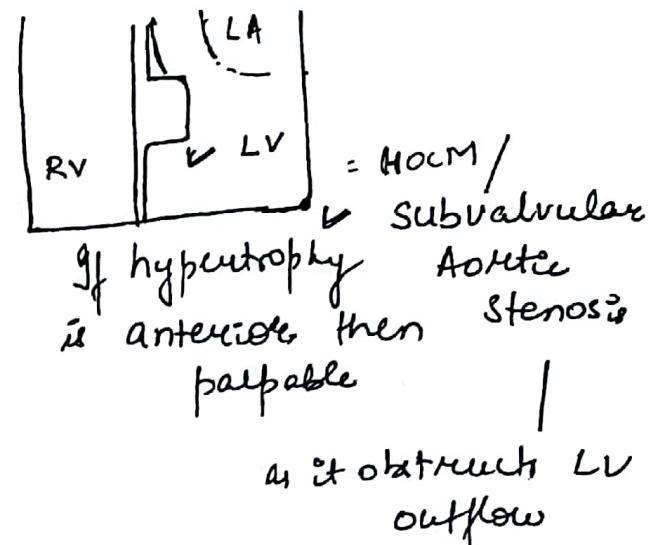
Area → < 2.5 cm² [localised].

Ab (N) of Apex

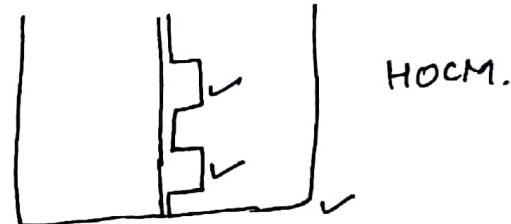
Ab (N)	Description	Cause
① Hyperdynamic	Palpable for upto $\frac{2}{3}$ of systole	(L) ventricular volume overload. [↑ co state]
② Sustained	Palpable for $> \frac{2}{3}$ of systole	(L) ventricle pressure Overload. eg. AS.
③ Diffuse	area $> 2.5 \text{ cm}^2$	Dilated cardiomyopathy
④ Double	2 impulses palpable in systole	LV aneurysm (complication of MI)



Asymmetrical Septal hypertrophy



⑤ Triple: 3 impulses palpable in systole



⑥ Absent non-palpable

Pericardial effusion
Emphysema
Obesity
Dextrocardia Q
↳ apex goes posteriorly hence not palpable

Q. Double Apex seen in
① AS [HOCM & subvalvular AS]

- ② TS
- ③ MS
- ④ AR.

AUSCULTATORY FINDINGS

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* S_1 .

due to closure of AV valve.

(N) $\Rightarrow M_1 T_1$ [mainly contributed by mitral valve].

Split < 20msec.

Site : Apex

* Pitch : moderate

Any mitral valve sound/murmur.

Best area = Apex

Ab (N)

Factors affecting
the intensity

soft S_1

Loud S_1

1) Force of isovolumetric ventricular contraction
if weak force
eg. Dilated CMP
LVF,
RVF
VSD

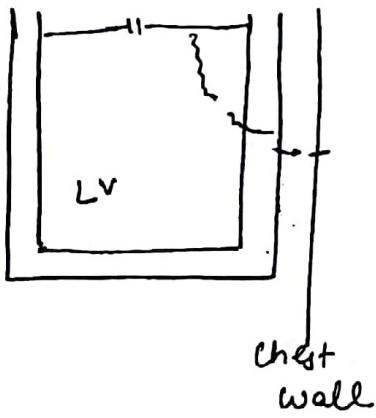
Strong force
eg. MS, TS
(if atrial P is high)

2) Condⁿ of A-V leaflets
if fail to strectch
each other

eg. MR
TR

calcification of
leaflet

3) The presence
of fluid,
m/s
air
fat
between AV leaflet
& stethoscope



- if ventricle blood
vol. ↑.

AR

PR

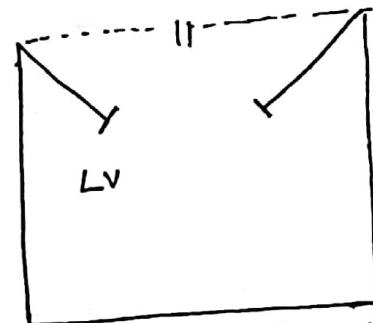
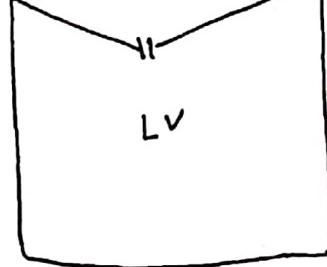
- if ventricle wall
thickness ↑
LVH ← AS
RVH. ← PS

thin.
lean.

LMR

All valvular Lesions cause
Soft S, except MS + TS

a) Most imp
factor
Position of AV
leaflets at onset
of ventricle
contrac.



If impulse reaches ventricle late
+ ventricular blood filling fully
complete
↓
AV leaflets forced to close
position.

If impulse
reaches ventricle
fast +
ventricle blood
filling incomplete
↓
AV leaflets fully
open.

- Bradycardia
- PR interval ↑

Tachycardia
short PR interval

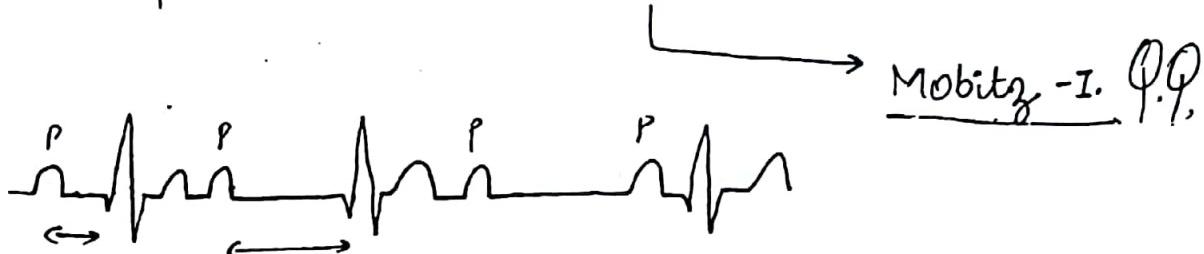
Q. In Hypothyroidism, S_1 is soft-

Q. In Digoxin effect, S_1 is soft ans AV Block \rightarrow PR ↑ interval

Q Condⁿ causing variable S_1 intensity :-

If variable HR = AF

Q If variable PR interval = 2° AV Block



Progressively PR interval ↑ till atrial impulse fails to conduct to ventricle
= Wenkebach's phenomenon.

* S_2

It is due to closure of Semilunar Valves.

(N) $A_2 P_2$

Aortic valve closes earlier than Pulmonary valve
 \downarrow

LV ejecⁿ time is less than RV

Site = For A_2

aortic area

For P_2 .

Pulmonary area

(R) 2nd Ics

(L) 2nd Ics

Best for S_2

\rightarrow Pulmonary area. [as both sound heard]

Split = 30-60 msec.

During Inspiration → split Increases

33



LV blood vol ↓

LV ejection time ↓

A₂ early

RV blood vol ↑

RV ejection time ↑

P₂ → Late

During Expiration → split Decreases or Expired



LV blood vol ↑

A₂ late.

RV blood vol ↓

P₂ early

~~WV~~
Ab N of S₂ split

① **Wide Split**



CAUSES

I) **Early A₂**. (earlier than physio limit)

If LV ejection time ↓

VSD

MR

or

If LV early depolarisation.

WPW syndrome

M/c site → L Q.

accessory pathway

from LA to LV will depolarise

LV early.

→ Type A WPW syndrome

Q (Bundle of Kent)

WPW SYNDROME

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- 1) ♂ > ♀
 - 2) L side more common
 - 3) short PR interval
 - 4) S, will be soft Q. -- ?

II) P_2 is Late [Later than physico limit]

② REVERSE SPLIT or P₂
PARADOXICAL SPLIT
CAUSES A₂

① P_2 is early (earlier than A_2)

(II) A_2 is Late

(later than P_2)

↓
LV ejec' time ↑

↓
LV Late depolarisation

AS

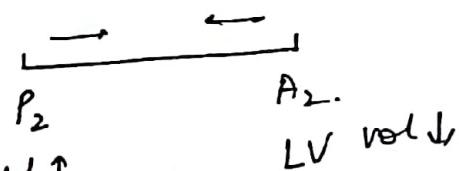
LBBB

LVF

Q. How to differentiate bet'n Split + Reverse Split.

During Inspiration.

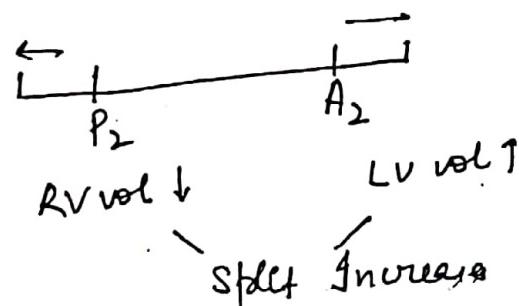
Reverse Split will Decrease RV vol ↑



split Decreases
[against N rule].

During Expiration

Reverse Split will Increase



split Increases

Q. In. Pulmonary artery HTN. S_2 Split

(A) ①

(B) ↑

(C) No change

→ P_2 comes early ---?

Hint - Pulmonary hang out interval

③ WIDE + FIXED SPLIT

doesn't vary \equiv resp. phases.

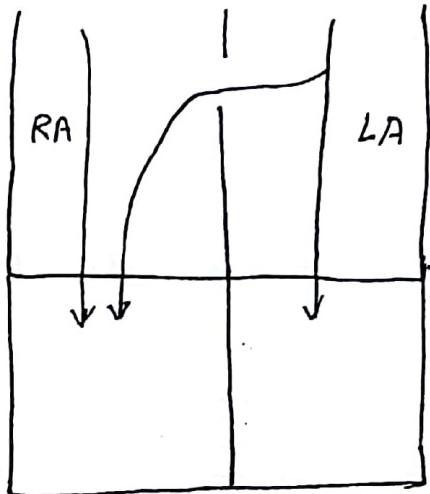
causes \rightarrow ASD.

RV blood $\uparrow \rightarrow$

P_2 late
 A_2 early

wide

LV blood $\downarrow \rightarrow$



Split is fixed

= ventricle blood vol
remain constant

during Insp. & Exp.



$$\begin{aligned} \text{RV blood} \rightarrow \text{Insp.} &= \uparrow + \downarrow \\ \searrow \text{Exp.} &= \downarrow + \uparrow \end{aligned} \Rightarrow \text{Fixed.}$$

Intensity of S_2

Factors

1) Pressure of aorta/
Pulmonary to close
SL valves.

2) Cond'n of SL valves
Leaflets.

Soft

Hypotension

Loud

Systemic HTN
 $\rightarrow A_2$

P. HTN $\rightarrow P_2$

calcified

AR

PR

x

* Single S_2 seen in

AR [A_2 is absent]

PR [P_2 absent]

AS/PS [valves get severely calcified]

S_3 / Ventricle Gallop

It is due to ↑ in ventricle blood volume during early filling phase.

↓
ventricle vibrations

Causes:-

↓

Systolic dysfunction
↑ end systole volume

① VF
RVF
DCMP
MI
LV aneurysm

Atrial venous filling ↑

↓ early filling phase
↑ blood will enter ventricles from atria
eg. high CO state
↓
MR • TR

Site → LV S_3 → Apex

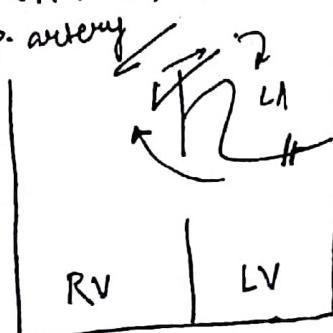
RV S_3 → Tricuspid area. [① lower parasternal]

Pitch → Low pitch.

Q. In atrial septal defect ← side S_3 → RV S_3 / LV S_3 ?

Ans → RV S_3 .

Q. In VSD, ← side $\bullet S_3$ = LV S_3



Pulmonary valve is open in systole so blood from RV goes into P. artery ↓

P. vein

↓
(L) atrium

MV is closed in systole & blood is collected in it ³⁸
1st chamber to enlarge is L atria.

Q. In PDA L side $S_3 = LVS_3$

S_4 / Atrial Gallop

It is due to atria contracting against stiff ventricles → ventricle vibrate

Causes -

- 1) Restrictive CMP
- 2) HOCM
- 3) LVH due to AS
- 4) RVH due to PS
- 5) Acute MI.

In acute MI Both $S_3 + S_4$.

↓ Relaxation

↑
↓ ATP due to ischaemia.

Site - $LVS_4 \rightarrow$ Apex

$RVS_4 \rightarrow$ Tricuspid area

Pitch - Low pitch.

Q. S_3 can be physiological -True/False

Ans → ♀ • young children • athletes

Q. S_4 can be physio - True / False

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Q. S_3 represents systolic failure

Q. S_4 represents Diastolic failure

Q. S_4 seen in all except

a) AS [LVH]

b) Constructive Pericarditis [ventricles are trapped \rightarrow can't vibrate]

c) AR \rightarrow extreme ventricle dilatation \rightarrow making it stiff

d) Amyloidosis [RCMP]

Constructive Pericarditis doesn't produce S_3 & S_4 .

ADDITIONAL HEART SOUNDS

Name

Ejection click

Cause

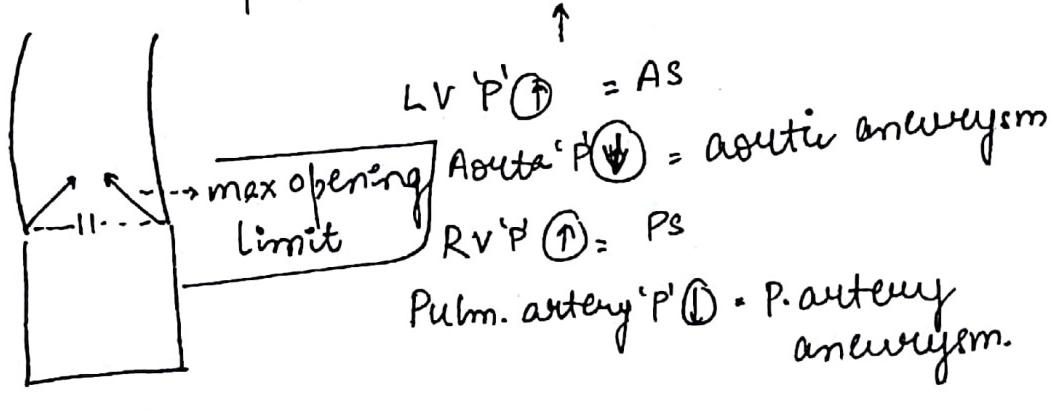
due to sudden
cessation of opening
of SL valves as it
opens = high pressure

Timing

s_1 s_2
early systole

Pitch

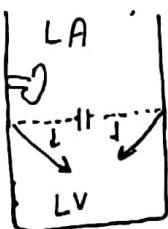
High.



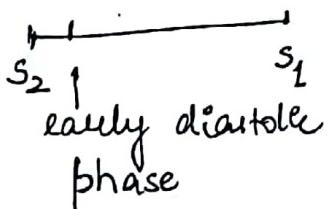
L:

Ejection click ↓ in calcified lesions.

2. Opening snap

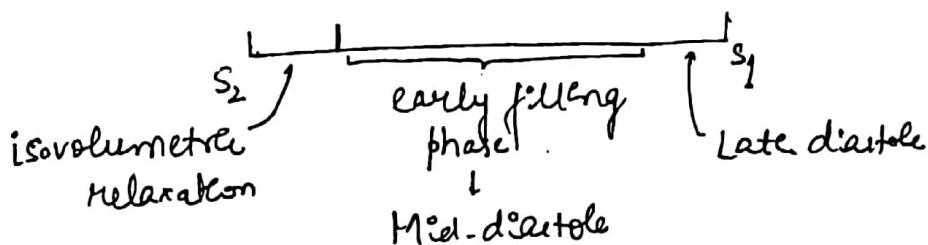


sudden cessation
of opening of AV
valve as it
opens in high pressure



High

LA pressure ↑ = MS, LA myxoma
RA pressure ↑ = TS



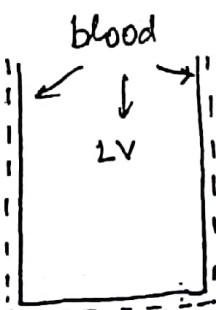
③ Tumour Polyp

① atrial myxoma
striking mitral valve

Early diastole

Low

④ Pericardial knock



ventricle walls
strike [knock] on
stiff pericardium

Early filling
phase

High

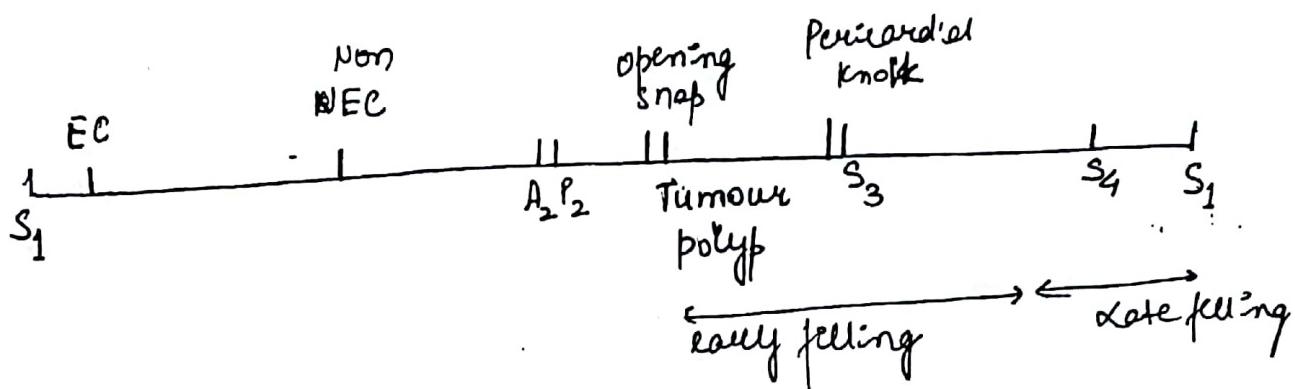
Most specific sign
of
constructive
pericarditis.

⑤ Non-ejection click

MVP collapse

≥ mid systole

High

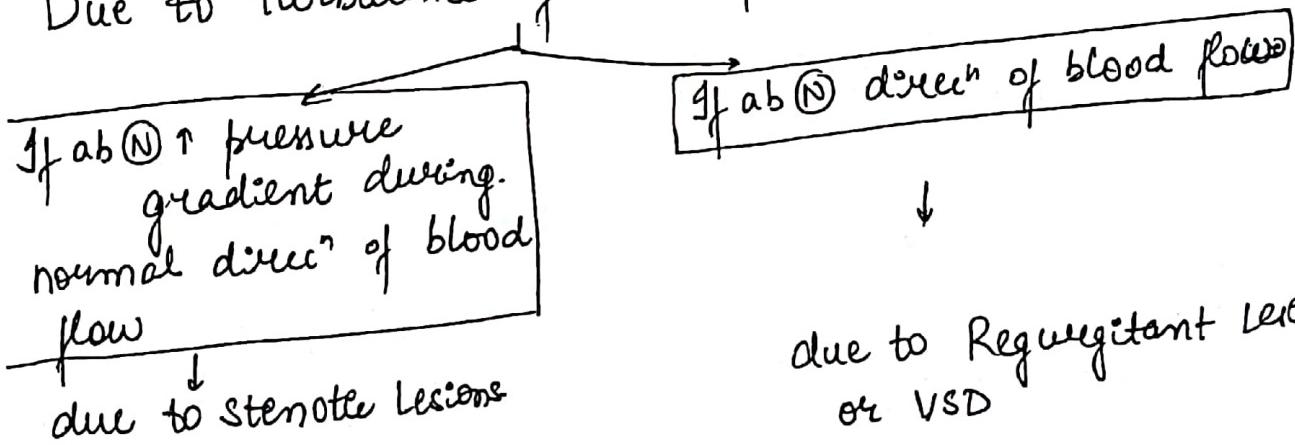


In AF. JVP = a wave absent

HS = S₄ ⊖ [if previously present]

MURMURS

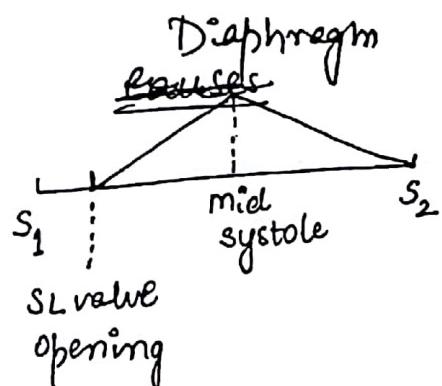
Due to turbulence of blood flow or the



TYPES

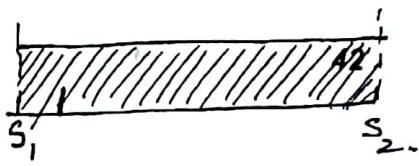
I) SYSTOLIC MURMURS

- Name M/c murmur overall Diagnose
- ① Ejection systolic murmur due to turbulence of blood flow due to ejection phase
- or
- Mid-Systolic murmur AS, PS
- or
- ↑ CO states. → [♀].
- or
- ↑ blood flow across SL valves (↑ blood flow across SL valves)
- or
- crescendo-Decrescendo



② Pansystolic murmur
No peak.

VSD
[LV pressure remain > RVP throughout systole]



chr. MR
[LV 'P' remain > LA 'P' throughout systole]
Chr. TR.

③ Early systolic murmur

If defect closer before mid-systole
e.g. Small muscular VSD



If pressure gradient become zero (\leq mid-systole)



(b) Acute MR.

[MI or IE]. LA is not dilated unlike Chr. MR.

During early systole, (L) ventricle blood enters LA

LA 'P' will ↑ rapidly

during mid systole (L) atrial 'P' = (L) ventricle 'P'
murmur will stop

(c) Acute TR.

④ Late systolic murmur

MR Prolapse



II

DIASTOLIC

MURMURS

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Name

Causes

1) Early Diastolic

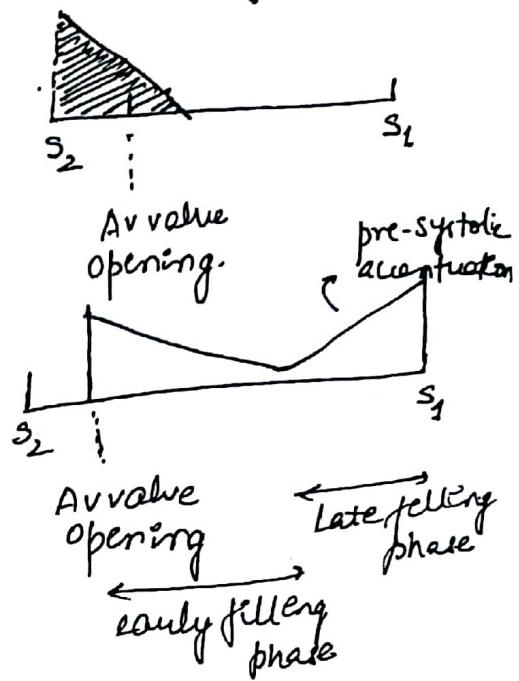
murmur.

OR

Decrescendo Murmur

AR, PR

Diagram



2) Mid-Diastolic murmur

Turbulence of blood flow from atria to ventricles.

MS, TS

Q. Early Systolic murmur seen in all except

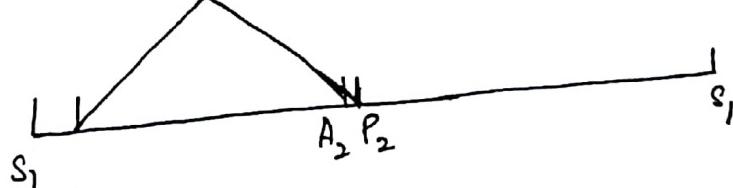
a) TR (acute)

b) VSD (small mural)

c) papillary m/s necrosis (MI \rightarrow acute MR)

d) AS

Q. Identify the valvular lesion



a) MS

b) TS

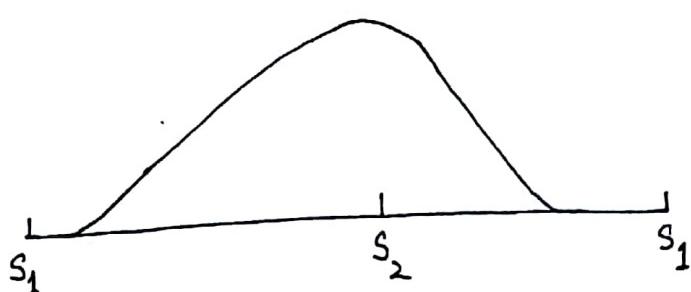
c) PS

d) PS

III

CONTINUOUS MURMUR

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- Starts in systole
 - Peaks around S_2
 - Ends in Diastole
- Origin - single site

Mechanisms :-

If Ab(N) pressure gradient is maintained throughout
Systole + Diastole
&

If Defect remains open throughout Systole + Diastole

Continuous murmurs are never due
to valvular lesions

[CAUSES :-

1) Ab(N) communication b/w artery to vein

e.g. A-V fistula

Ruptured sinus of valsalva
(acute to RAtria connection)

2) Ab(N) communication b/w systemic to PULM

e.g. PDA

(3) ↑ blood flow into blood vessels
 mammary artery souffle (lactation) 45
 uterine artery souffle. (♀)

(4) Severe arterial stenosis [$>70\%$ narrowing of diameter]
 Renal artery stenosis → bruit

Q. Continuous murmur can be physiological - True/false
 4 Q, Lactation

Q. All causes continuous murmur except:

a) pt. of CKD on haemodialysis [A-v fistula]

b) severe atherosclerosis (carotid or renal artery stenosis)

~~c) AR + AS~~

d) Lactation.

D/D of Continuous MURMUR.

Continuous murmur

To & fro

Systolic-diastolic

Systole



+ Diastole

Origin

single site

single Site

Different sites

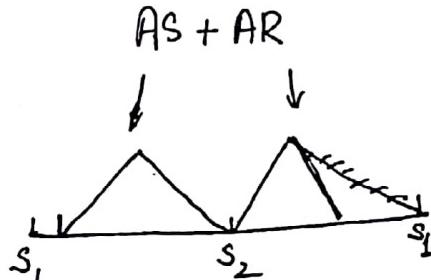
Peak around



S_2

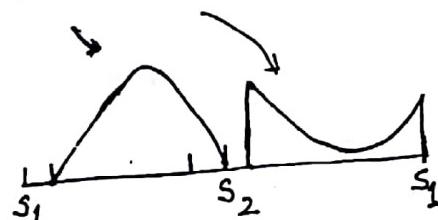


AS + AR

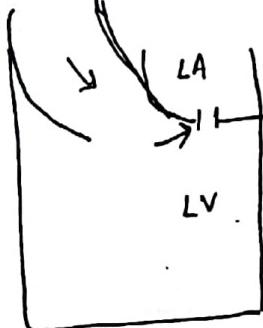


e.g.

AS + MS



Name	Cause	Type	Site
1) Gibson's murmur	PDA	continuous	(L) upper parasternal area 46
2) Key Hodgkin's murmur	AR	early diastolic	(L) 3 rd ICS = Ekb's area = Neo-aortic area
3) Graham-Steel's murmur	PR	early diastolic	(L) 2 nd ICS Pulmonary area
4) Austin Flint murmur	AR	mid-diastolic to late	Apex
	Regurgitant jet of AR striking mitral valve.		
5) Carey Coomb's murmur	ARF	mid-diastolic murmur.	Apex
	Turbulence of blood flow over inflamed rough mitral valve		
6) Dock's murmur	Severe stenosis of LAD artery (widow's artery)	continuous murmur.	3 rd (L) ICS Gum from sternal margin



⑦ Still's murmur
→ Innocent murmur

young children

Ejection systole murmur

Pulmonary area

(relatively ↑ blood flow across Pnlm. valve)

⑧ Rytand's murmur

complete AV Block.

↑ Blood flow across AV valve

mid-diastolic

apex.

FACTORS AFFECTING MURMURS:-

If blood flow ↑ → all murmur will ↑

except

↓ MVP

HOCM.
Murmur

Blood flow

1) Respiratory variation.

a) Inspiration

↑ blood on (R) side

b) Expiration

↑ blood on (L) side

c) Valsalva effect
(Persistent expiration)

Persistent expiratory
↓ blood on (R) side
followed by (L) side.

↑ TS, TR, PS, PR
exception

Pulmonary ejection click
↓ in inspiration

↑ MS, MR, AS, AR

[Except HOCM, MVP]

All murmur will ↓
[Except HOCM, MVP].

II Postural Variation :-

a) Standing

↓ blood flow into R+L side

48

all murmur will ↓
except HOCM, MVP

b) squatting
(immediate effect)

↑ blood flow into R+L side

all murmur will ↑
except HOCM, MVP

III Effects of Afterload changes :-

Lesion

Afterload ↓
(aorta 'P' ↓)

Afterload ↑
(aorta 'P' ↑)

AS

murmur ↑

murmur ↓

Pressure gradient

$$= \frac{LV}{'P'} - \frac{aorta}{'P'}$$

AR

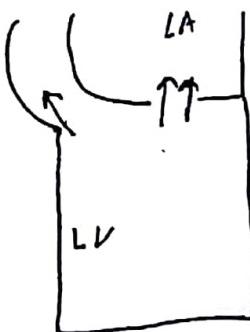
murmur ↓

murmur ↑

Pressure gradient

$$= \frac{aorta}{'P'} - \frac{LV}{'P'}$$

MR



Regurgitant lesions behave similar

MVP

49

Cause: Deficiency of type III collagen in MV leaflets (posterior)
 ↓
 ↑ leaflet flexibility
 ↓
 surface area of MV leaflet ↑
 ↓
 too big for LV cavity

C/F.

Symptoms :-

- 1) Chest pain
M/c symptom.
Due to papillary m/c stretching

- 2) Palpitations

ventricle fibre stretching

↓
produce ventricle ectopic

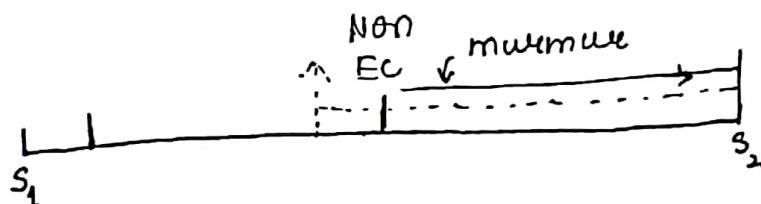
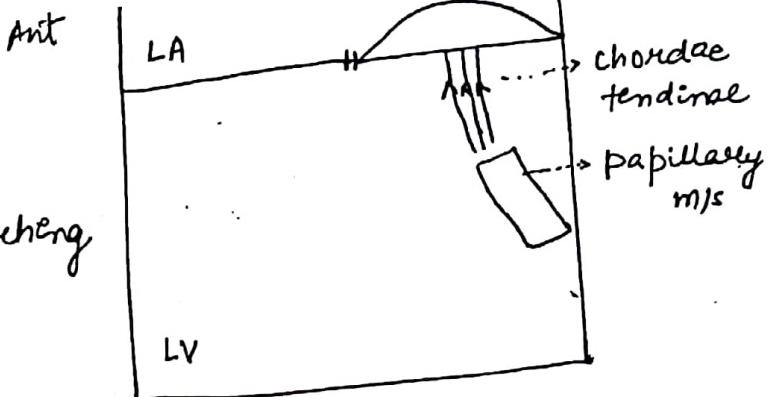
sign :-

► M/c sign → **Non-ejectⁿ diet.**

due to doming of MV
It occurs when LV cavity size ↓ significantly

- 2) Late systolic murmur (MR)

occur when post. leaflet looser contract c ant. leaflet.



If LV cavity blood vol. \downarrow \rightarrow Prolapser will occur early
[standing position]
inspiratory phase

\downarrow
Non-eject⁶⁰ click earlier.

\downarrow
murmur will start earlier

[Jnv]

2D Echo
if prolapsus is $> 2\text{mm}$ into LA

[T/t]

1) Reassurance. (mostly benign)

2) β blockers (if palpitations) DOC

3) Sx Repave \leftarrow NYHA symb $\geq II$

+
Severe MR on Echo.

HOCM

51

Cause - AD

mutation of β -myosin heavy chain.
["Private mutations"]



Asymmetrical proliferation of septum.
near the LV outflow tract.



Free wall hypertrophy



LV systolic function ↑
to overcome obstruction

Diastolic func'
 \downarrow as filling
is impaired

C/F

Symptom :-

1) Earliest → Dyspnoea \leftarrow LAP↑ \leftarrow LV'P↑

2) Angina \leftarrow ↑ LV workload.

+
Coronary vessels compressed by hypertrophied myocytes

3) Syncope



Fixed CO [CO will not ↑ during demand]

4) * Sudden cardiac death

→ Irreversible loss of cardiac funcⁿ

in 1 hour of symptoms

→ HOCM is M/c.

→ SCD is due to ventricular arrhythmias due to ischaemia



② Na^+/K^+ atpase

Signs :-

1) Pulse = Bifid
or
Pointed finger pulse

⇒ JVP =

If hypertrophied septum bulge
into (R) atrium

Bernheim's effect Systolic func[↑] - Brisk rovol. → Percussion
↓ confere["] wave will
 be early

RV 'P' T

- $a \uparrow$
 - y slow

3) Apex = Double / Triple

4) s_1 = Intensity Soft

$S_2 = \text{split Reverse}$

$$S_3 = \text{None}$$

$$S_u = LV S_u + t$$

Lv ejection time ↑
(due to obstrn")

99

5) Most characteristic sign :-

Type → ejection system

Site → (L) 3rd ICS Emb's area



(SAM)
systolic ant. movement of mitral valve towards septum
further ↑ ring the obstacle.

2 most imp factors affecting obstruction

Drug

① Contractility

if ↑ → SAM ↑ → obstruction ↑

Digoxin. C/I in HOCM.

② Blood in LV if ↓ → obstruction ↑

(preload)

Diuretics
Veno Dilators

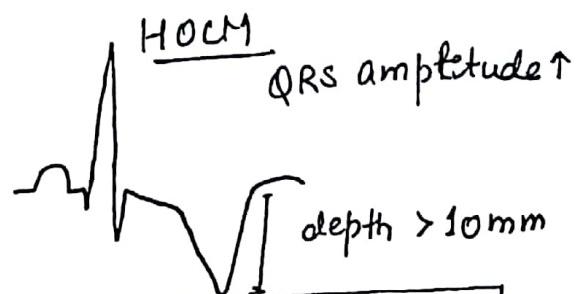
(Blood act as physical barrier separating MV & septum)

Find

1) CXR → cardiac size (N)

2) ECG →

⇒ (N)



3) Echo - $\frac{\text{septum thickness}}{\text{LV free wall thickness}}$

$\frac{3}{1}$ [reversed from (N)]

RX

54

- 1) β blocker \rightarrow Initial DCC
If CI \rightarrow Non DHP CCB.
Doesn't prevent sudden cardiac death.
- 2) AMIODARONE
given if post H/O ventricular arrhythmia
- 3) Implantable defibrillator Device (intracardiac)
 \hookrightarrow prevent SCD
- 4) Septal artery sclerosis [ethanol]
 \downarrow
causes regression of septum.

LMP

ARF

12/2/18

55

Cause:-

Hypersensitivity reacⁿ to Group A β haemolytic Streptococci [Pharyngitis]
Type II MSN Reacⁿ.

C/F & Inv:-

Modified Jones Criteria

Major:- (5)

unique features

Rx

DOC - Aspirin

75mg 1kg/day

① Arthritis

M/c major manifestation

Large joints

asymmetrical

migratory

Non-erosive (non-deformity)

Polyarthritis

Duration ≤ 4 wks

Exception - JACCOUD's
arthropathy
(deformities +)

② Carditis

M/c valvular
Lesion in
RHD = MS

M/c c of Death = CHF

M/c larger = Endocarditis

M/c valve = Mitral

M/c Lesion = MR

L/c valve = Pulmonary

Hypocarditis = no necrosis
[Troponin - N]

Pericarditis → Tamponade
Constructive Pericarditis] very rare

Date Diuretic
↓ no response
Steroids
↓ no response
Value replacement

③ Sydenham's Chorea

[Ab against basal ganglia, cerebral cortex]

- Motor = Tongue
fibrillation +
 - Ext. Rotation of hand.
["scooping"] +
 - "Milking action"
 - Disappears in sleep
 - $\text{♀} > \text{♂}$
 - Late manifestation.
 $> 1-7$ months
 - Neuro-psychiatric disorders
- Sedation
 ↓ no response
 Valproate.
 ↓ no response
 IV Ig Q.Q.
 (for refractory cases)

④ Subcutaneous Nodules

Site = extensor surface
Non-tender
Size - 0.5-2 cm

No t/t required

⑤ Erythema Marginatum

Site - extremities
Trunk
(never on face)
Serpentine edge
progress fast



Minor Manifestation

- Clinical
- 1) Fever (M/c Symptom)
 - 2) Antihistamines

Lab

- 1) ↑ ESR
- 2) ↑ CRP
- 3) ↑ PR interval on ECG.
- 4) [due to AV node inflammation]

Essential Criteria

- 1) Evidence of recent streptococcal infec"
(<45 days)

h/o scarlet fever
is removed now.

Any one of 3 criterias -

a) throat culture +ve

b) Ab +ve for [ASO ↑ &/or Anti DNase]

c) Rapid streptococcal Ag test

Minimum criteria needed to make Δ of

Clinical

Major

Minor

Minors Essential

1) 1^o ARF

2 major

1

-

or

2

~~1~~ +

+

2) Recurrent ARF

3

+

3) Recurrent ARF

on established RHD

2

+

4) Sydenham's chorea

-

-

5) Indolent Carditis

-

-

-

(~~out any kn cause~~)

Changes in Jones Criteria.

58

↓
Low Prevalence
ARF < 2/1 lakh school
going children

High Prevalence
72/1 lakh [India].

Major

Joint Involvement
= Polyarthritid

Polyarthritis
or
Monoarthritis
or
Polyarthralgia

Minor

Fever $> 38.5^{\circ}\text{C}$

$> 38^{\circ}\text{C}$

Arthralgia - Polyarthralgia

Monoarthralgia.

ESR $> 60 \text{ mm/hour}$

$> 30 \text{ mm/hour}$

Prophylaxis :-

1) 1^o Prophylaxis :- Streptococcus → ARF
pharyngitis

⇒ [Ab of choice] = Benzathine Penicillin Single Dose
(1.2 mU) if $> 27 \text{ kg}$
~~if ≥ 27~~ 0.6 mU if $< 27 \text{ kg}$.

Should be started less than 10 days of Pharyngitis
↓
of penicillin allergy

Macrolides (erythromycin or azithromycin)

27 2° Prophylaxis ARF → Recurrent ARF

Ab of choice = Benzathine Penicillin.
(1.2 or 0.6 ml)

59

every 3-4 wks

↓ if allergy to penicillin

Sulfadiazine Q

↓ if allergy

Macrolide

Duration of 2° prophylaxis.

Clinical 1

ARF → out
carditis

1) 5 years or till pt's age 21 yrs
[if ever is longer]

ARF → carditis

2) 10 yrs or till pt's age 21 yrs.
[if ever is longer]

ARF → RHD established

3) India - Lifelong ideally
10 years till pt's age 40 yrs
(if ever longer)

D/D of ARF :-

1) Post-Streptococcal Reactive arthritis (PSRA) :-

- Small joints
- Symmetrical
- Duration > 1 month.
- Poor response to aspirin.

27

- (2) P - paediatric
 A - autoimmune
 N - neuropsychiatric
 D - Disorder
 A - associated i
 S - streptoc.
- NO other ARF manifestations ⁶⁰

Complications of ARF.

VALVULAR HEART DISEASE.

MS

Cause - M/c - RHD

M/c non-rheumatic
 = congenital

Pathophysiology:

↑ LA 'P' (dysphoria early symptom)
 ↓

↑ Pulm. Vein ↑
 followed by

↑ Pulm. artery 'P'

↓
 RV pressure overload.
 ↓ remodelling

RV [concentric hypertrophy]

↓ Later

RV systolic failure

↓
 RV blood retention occur

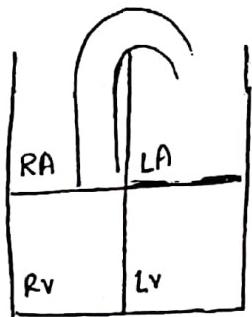
↓
 RA 'P' ↑ ← Systemic vein 'P' ↑

2nd site of stenosis → Pulmonary artery.

MR

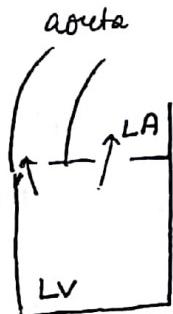
M/c - RHD

M/c non-rheumatic
 = MVP



↓ CO

↓
 Gradual LA dilatation.



↓ during diastole

↑ blood will move from LA to LV

↓
 LV volume overload.

↓ remodelling

LV eccentric hypertrophy

COT

↓ later

LV systolic failure

↓
 LA 'P' ↑

Symptoms Mech
 ① Dyspnoea \leftarrow LA P'↑

② Haemoptysis \leftarrow M/c source
 = Bronchial vein

③ Anasarca \leftarrow Systemic veins
 hydrated P'↑

④



④ Recurrent
 laryngeal n/v

Hoarseness of
 voice

[Ortner's syndrome]

Signs

Pulse - irregularly irregular
 rhythm

Pulse Deficit

Due to AF →
 Pulse

(+) (+)

(+) (+)

JVP →

Reversal
 occur

Absent Prominent
 a b
 x y

due to AF

Apex - LV (N)

Site - (N)

Nature - Tapping

LV - Dilated + vol. overload

Site - shifted laterally

Nature - Hyperdynamic

Auscultatory signs

S_1 = Loud
exception - if calcified valves

S_1 = soft

62

S_2 = split - wide

S_2 = split - wide

if RVF occur $\rightarrow P_2$ late.

LV ejection time ↓ = A_2 early

S_3 = never LVS₃

S_3 - LVS₃ ++

if RVF $\rightarrow RVS_3$ +

S_4 = if RVH $\rightarrow RVS_4$

S_4 : LVS₄ ± [in late MR due to extreme LV dilatation making it stiff]

Opening = +ve snap

Opening = -ve snap

becomes ⊖ if calcified valves

Murmurs

①°

Type = mid-diastolic

①°

Type = pan-systolic

Acute MR = Early systolic

MVP induced = Late systolic

Site - Apex

Site - Apex

Pitch = Low pitch

Pitch - High pitch

If pressure gradient < 40 mmHg
= low pitch murmur

Stenotic lesions are low pitch
Regurgitant " are high pitch

Radiation - Nil

Radiation - Interscapular area
Axilla

Best pt's position - ④ Lateral decubitus

Best pt's position - ④ Lateral decubitus

Phase - Expiratory

Phase - Expiratory

2° murmur = -

Clinical Criteria for severity

- 1) Opening snap
 S_2 -OS gap inversely related to severity



- 2) Length of murmur is directly related to severity

I_x

ECG- sequence

- ①(L) atrial enlargement



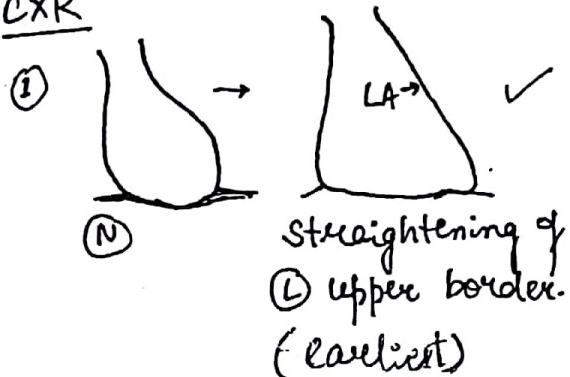
- ② RVH signs



- ③ RA enlargement

Btrial enlargement
= due to Ms

CXR



2° murmur

↑ blood flow across MV₆₃ during diastole due to ↑ blood.

= mid-diastolic murmur

= **Functional Ms** → severe MR

1) Apex = shifted laterally

2) S_2 = wide split

3) S_3 = trace of LV S_3

4) murmur = mid-diastolic

Loudness or intensity is never a criteria for severity in Valvular Heart Disease

I_x

ECG

- ① LAE

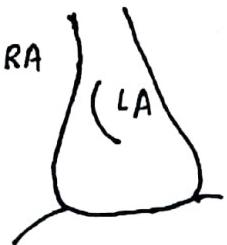


- 2) RHT signs LVH signs.

CXR

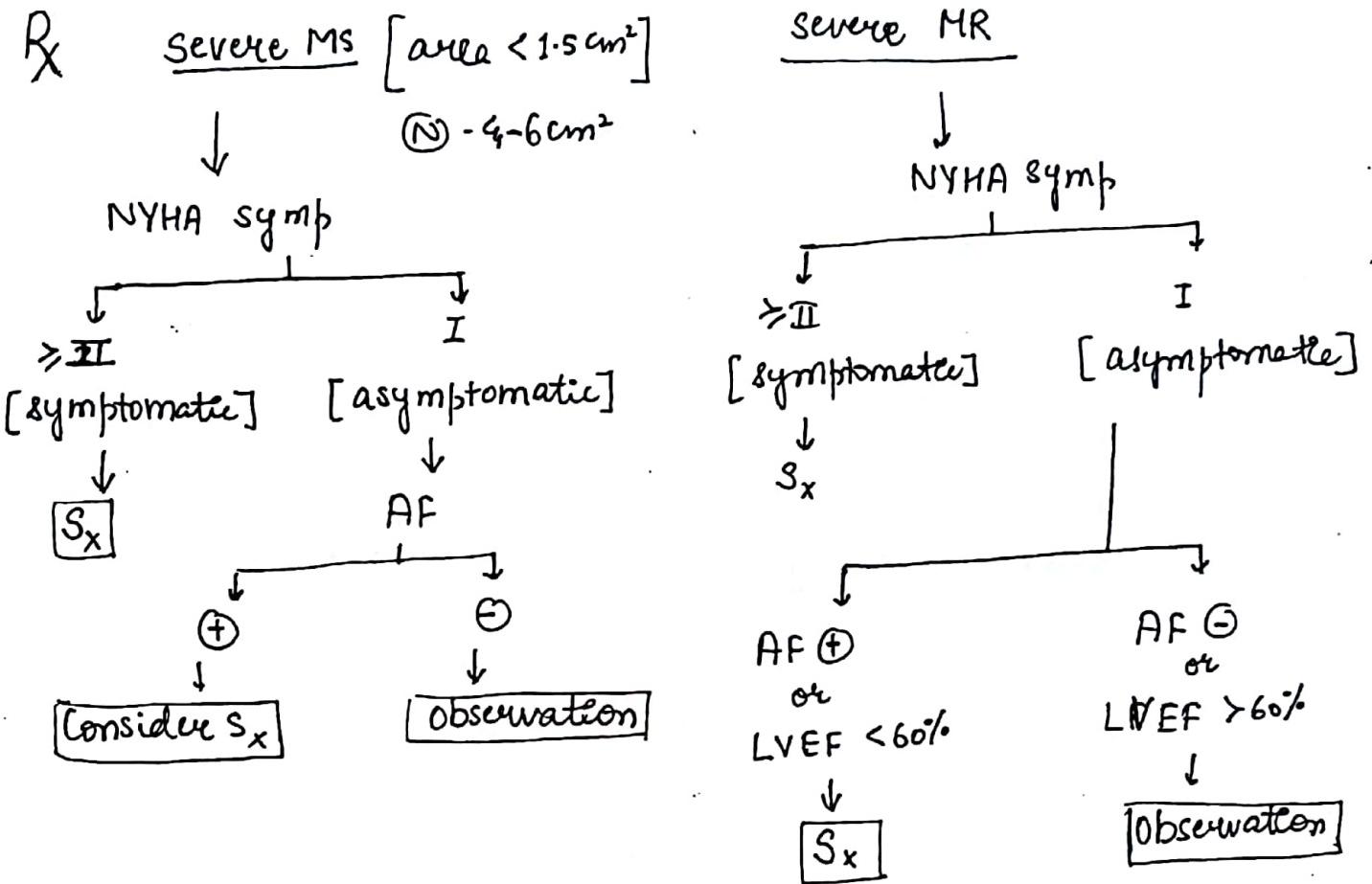


② Double atrial shadow



very rare.

64

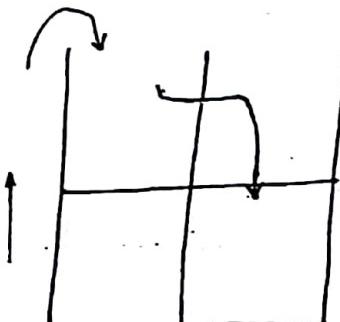


S_x

Preferred S_x / Initial Process of choice / S_x in ♀
Balloon valvotomy

Preferred S_x = MV Repair

If not possible
MV Replacement



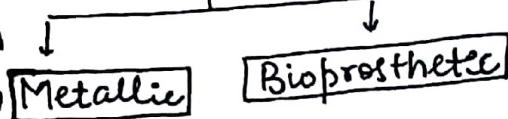
IVC Done under Lung-Heart Bypass machine.

Criteria:

- 1) Isolated MS
- 2) No calcification
- 3) No LA Thrombus

↓ if not fulfilled

MV Replacement



Dur. 25 yrs 5-10 yrs

Anticoagulation X
= lifelong

Age Preference
= young elderly

Q. 26 yr old, unmarried ♀ . K/c/o RHD c MS
c/o - dyspnoea on 10 steps . Echo = MVA 0.8 cm^2 .

Next Line Rx

- observation
- balloon valvotomy
- Bioprosthetic, MV replacement
- Metallic, MV "

Q. same history. O/E - opening snap (+ve.)

ans - (b)

Q. Same history, O/E - Pulse Deficit +20, opening snap (-nt)
calcification.

ans - (d)

Q. Same history. marred, Q.E - opening snap (B),

MR +

66

Ans → (d)



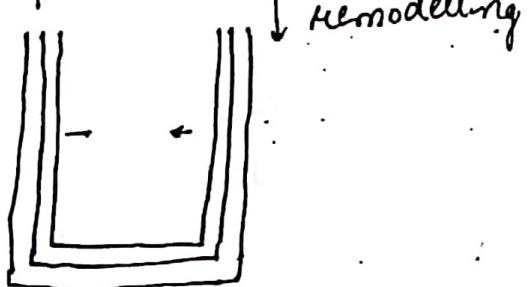
Give heparin in 1st Trimester
anticoag in 2nd Trimester - 3rd
heparin in ~~3rd~~ " delivery.
2 wks prior to.

AS

Cause - H/c age related calcification

Pathophysiology :-

LV pressure overload



LV (concentric) Hypertrophy

↓ later

LV systolic failure

↓
LA 'P' ↑

Symptoms :-

→ Daze to

→ Angina ← ↑ LV workload → Palpitations ← LV force of contraction ↑

Mech.

2) Syncope ← fixed co

2) Angina [Nocturnal]

← ↓ in Diastolic BP $\underline{\text{BP}}$ leads to less perfusion

This occurs more during night as sympathetic activity ↑ further ↓ vascular tone.

3) Dyspnoea ← LA 'P' ↑

[Worst Prognosis]

Mortality \bar{c} in $1\frac{1}{2}$ yr even \bar{c} medical tht

Signs:-

→ Pulse - Most specific
Pauvre et tardive

2) Apex - LV 'P' overload

↓
Site = N

Nature = Sustained

3) S_1 = Soft

S_2 = split = reverse

LV ejecⁿ time ↑ → Late A_2

in early stages → narrow split

S_3 = + if LVF occurs

S_4 = ++

Ejection click = +

3) Dyspnoea ← LA 'P' ↑

Most specific.

= Bisferiens

LV Dilated + vol. overload

Site = shifted laterally

Nature = Hyperdynamic

S_1 = soft

S_2 = Single P_2 .

aorta valve leaflets fail to strike.

S_3 = ++

S_4 = + Late AR.

(-)

47 1° Murmur

Type: Ejection Systolic murmur Type: Early diastolic

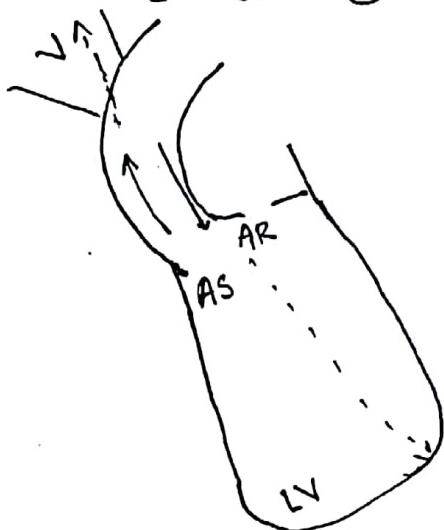
Site: (R) 2nd ICS [Aortic area - 1st]

68

Site: (L) 3rd ICS [Erb's Area]

2nd Aortic Area
or

Neo-aortic area



Pitch: Low

Pitch = high

Radiation: Common carotid
[or neck]

Radiation = towards apex

after striking arch of aorta

if radiation to axilla

Radiation to apex

= COLE - CECIL MURMUR

= GALLAVERDIN PHENOMENA

Best Pt's Position =
Leaning forward. ✓ ✓

Phase - expiration ✓

2° Murmur

Not seen in AS

↳ Austin-Flint murmur
mid- Late diastole

↳ Functional AS

T: Blood flow across
aortic valve

[ejection Systole].

Clinical Criteria for Severity

- 1) S_1 = Soft
- 2) S_2 = Reverse split
- 3) S_3 = \oplus
- 4) S_4 = \ominus

* Severe Silent AS

- \Rightarrow associated MS
- \Rightarrow LVF

\downarrow CO
Hence sound \ominus

I_x

[ECG] = Sequence
① LVH signs

② LA enlargement



ST Depression
T inversion

→ Strain pattern

[CXR]

Cardiac Size = \textcircled{N}

Rx

Severe or severe
AS AR
Similar

[Area $< 1 \text{ cm}^2$]

↓
NYHA symptoms

$> II$ (symptomatic)

1) Any peripheral sign of AR
 \Rightarrow Pulse - Bisferiens

3) Aper - Displaced Laterally

4) $\pm S_1$ - soft

5) S_5 - \oplus

Q 1° murmur = Duration.

\Rightarrow Presence of 2° murmur
= Austin-Flint murmur

[ECG] = sequence

① LVH

② LA enlargement



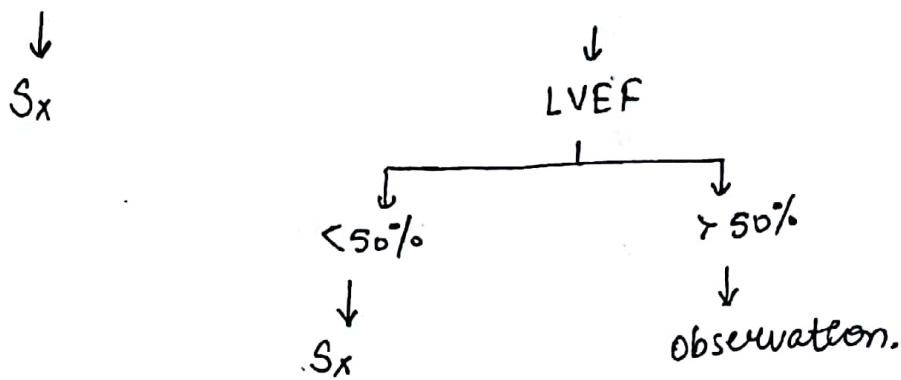
ST Normal
T upright

as inner myocytes receive blood from cavity

[CXR]

enlarged

I (asymptomatic)



Preferred S_x = Aortic Valve Replacement

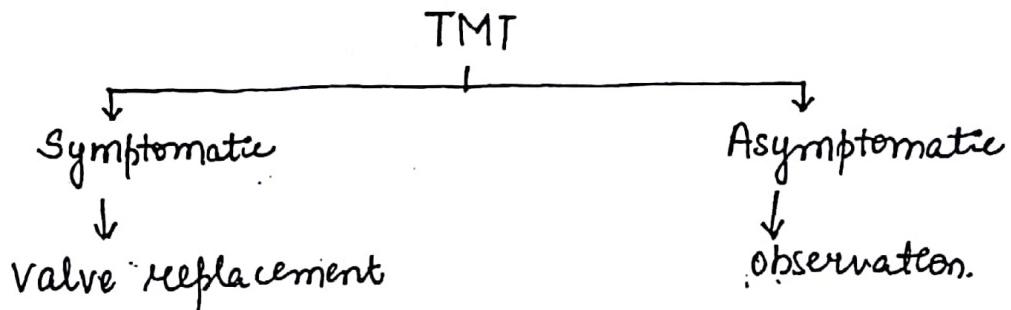
Q. 60yr old ♂, \in Aortic valve pressure gradient of 60 mmHg
 k/o AS, c/o - equivocal dyspnoea symptoms
 Next step?

- Ans.
- observation
 - Treadmill test
 - Aortic Valve Replacement
 - Diuretics.

Q. Same pt underwent treadmill test [Bruce Protocol]
 c/o Dyspnoea & Fatigue at 11 min of exercise

Next step

Ans.



Bruce Protocol

Bruce Stage

I

Duration

71

0 - 2:59 min

II

3 - 5:59 "

III

6 - 8:59 "

IV

9 - 11:59 "

Pt. considered symptomatic if c/o dyspnoea / fatigue

\leq Stage II

Asymptomatic if c/o dyspnoea / fatigue

$>$ Stage III

* Severe AS + NYHA-I + underlying CABG = Aortic valve Replacement

(R) SIDED VALVULAR LESIONS

Lesion

M/c Cause

Other cause

1) TS

RHD

(X)

2) TR

RV dilatation.

[eg. Pulmonary embolism]

cor-pulmonale

M/c Valvular Lesion
due to CARCINOID

3) PS

Congenital

Carcinoid
Rubella

4) PR

Press PAH

Carcinoid

Valve fibrillation

→ Regurgitation

Ring fibrillation

→ Stenosis

L/MR

INFECTIVE

ENDOCARDITIS

72

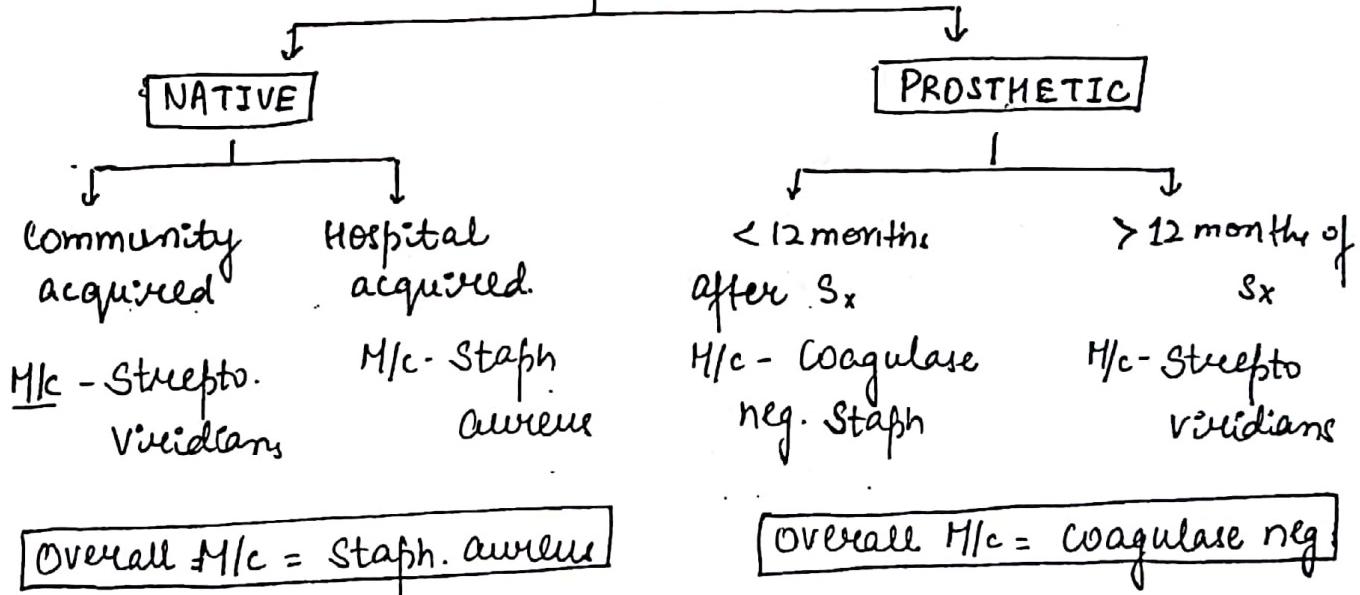
[AUSE :-

Predisposing Causes

- 1) M/c Valvular Lesion = MR > AR.
- 2) M/c congenital HD = VSD [R ventricle has vegetation]
- 3) M/c cyanotic cong. HD = TOF [L ventricle has vegetation]
 - ↳ systemic embolism.
- 4) Least common HD leading to IE = ASD
- 5) MC non-CV risk = " " " = IV Drug Abuse

Micro-organisms

* According to nature of valve affected.



HIV is the only virus to cause IE.

* According to Onset of

73

↓
Acute

[<2wks]

M/c = Staph aureus

Other

Strepto β-haemolytic

Fungus

Subacute

[>2wks]

M/c = Strepto. Viridans

Other

Staph coagulase neg.

Fungus

* Typical Bacteria of IE

1) Strepto Viridans

2) " Bovis [Gallolyticus] → ass/ε Colonie Cancer/Polyp.

3) Staph aureus → M/c in IV Drug Abuse → (R) sided

4) Enterococci → M/c in IV Drug Abuse → (L) sided.

5) HACEK group

C/F + Ix

Modified DUKE's Criteria

2 MAJOR

5 MINOR

3 EXCLUSION

* Major Criteria -

(1) Evidence of micro-organisms consistent c IE.

1) ≥ 2 Blood culture + of Typical Bacteria
OR

2) Persistent Bacteremia of micro-organism consistent c IE.
OR

≥ 2 Blood culture +
[separated by 12 hours]

≥ 3 Blood culture +
out of ≥ 4 samples
[1st & Last sample separated by 1 hr]

37 > 1 Blood Culture } of Coxiella Burnetii
or
IgG T

74

(II) Evidence of Endocarditis [ECHO]

- ↓
Endo
① Oscillating Mass Lesion. on valve or its structure
or
② Intra-cardiac abscess
or
③ New valvular regurgitant lesion \leftarrow M/c CVS
complication of IE.
or
④ Partial Dehiscence of prosthetic valve

* Minor Criteria

- 1) H/o Predisposing cause = RHD, I.V. Drug Abuser.
2) Fever $> 38^\circ\text{C}$ \leftarrow M/c symptom
3) Immune phenomena = R.R.O.G.
R \rightarrow Roth's Spots \rightarrow Immune complex vasculitis in Retina
Oval
Pale centre. \in haemorrhagic margin

Other causes -

a) SLE

b) CLL

c)

O \rightarrow Osler's Nodes \rightarrow Immune complex deposition
Finger tips / Palms / Soles.
Tender
Palpable.

G → GN → Immune Complex deposited in
S. C₃ levels ↓

75

R → RA factor +ve

4) Vascular Events

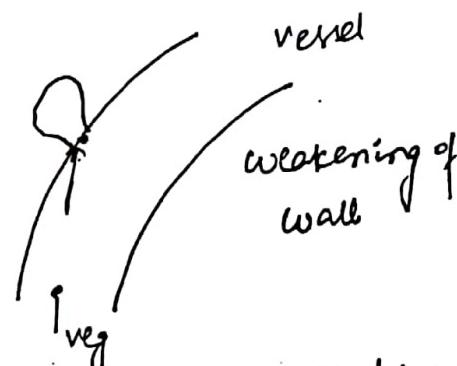
* Major Arterial Embolisation

[L sided] M/c site → Brain [MCA territory → Paralysed]
→ Spleen
M/c organism → Staph Aureus
M/c valvular IE → Mitral valve

* Septic Pulmonary Infarcts

[R sided].

* Mycotic aneurysm



* Haemorrhagic stroke [if mycotic aneurysm rupture in
Brain ↳

* Conjunctiva petechiae.

M/c Peripheral Sign of IE.

* Janeway Lesion = Palms.

Macular [non-palpable]

Non-tender

5) Blood Culture Positive of micro-org consistent w/ IE
(not satisfying major criteria)

or

Serology +ve.

Definitive Δ of IE = 2 Major

or

1 Major + 3 Minor

or

ALL 5 minor

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* Exclusion Criteria

- 1) Firm alternate Δ of Fever established.
- 2) If fever subsided \leq 4 days of Antibiotic Use.
- 3) If there is no histopathological evidence of IE < 4 days of Antibiotic Use.

Rx + Prophylaxis of IE = given in supplement

14/2/18

CARDIOMYOPATHY

77

Definition :-

Diseases of endomyocardium

Not due to valvular Heart disease.

↳ Cong. Heart disease

↳ HTN

↳ Ischaemia

↳ Pericardial Disease

Types :-

Dilated CMP (M/c pattern)

HOCM

Restrictive
CMP (Least common)

I Defect:

↓ contractility

Obstruct " to LV outflow
↳ overcome obstruction

failure of relaxation

↓ in diastolic func "

↓ in systolic func
+
Preserved diastolic
func " till late
stages

↑ in systolic func
+
(↓ cavity space)
↓ diastolic func

↓ systolic func
preserved.

Gross atrial
Dilatation

DILATED CMP

CAUSE -> Idiopathic (M/c cause)

Rx - supportive. [chr. HF = low EF]

Mc 2° cause - alcohol

Mech :- a) Direct ethanol effect

b) Becoz of Cobalt [cardiotoxic agent]

(foam ↓ stabilizing agent)

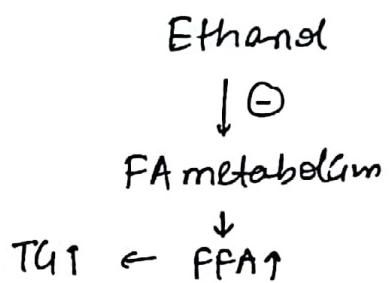
- Risk :- Mutation of alcohol dehydrogenase
 • Mutation of ACE (?)

Dose of alcohol = $\geq 120 \text{ gm/day}$ for 5-10 years

Rx = reversible in 3-6 months of cessation.

Other CVS manifestations of alcohol ($\geq 30 \text{ g/d}$)

- 1) Dyslipidemia
 a) $H/c = \uparrow TG$
 b) $\uparrow HDL Q.$
 c) $\uparrow LDL$



- 2) Effect on BP
 Acute - vasodilatation = $\downarrow BP$
 Chronic - (+) sympathetic system = $\uparrow BP$

- 3) CVS events
 a) CAD $\rightarrow \downarrow \text{risk by } \uparrow HDL$ [French paradox]
 b) stroke $\rightarrow \uparrow \text{risk}$ due to $\uparrow BP$

(*)

- 4) Arrhythmia
 alcohol binge $\rightarrow AF$ [Holiday Heart Syndrome]

III) Genetic Causes

MOI

1) AD

Q. Gene/Protein

TTN / Titin

↓
Sarcoplasmic protein. (N)
helps in contractile

Unique feature
₇₉

M/c genetic cause of
DCMP.

2) AR

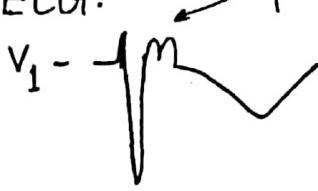
DSP / Desmoplakin

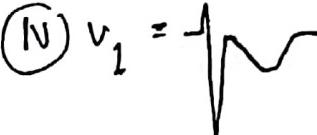
↓
Desmosome protein
(N) helps in synchro.
contractile

Arrhythmogenic
RV Dysplasia. (ARVD)

↓
sudden cardiac death
in young population.

- { wooly hairs +
thick palmar skin +
ARVD 

ECG. 
V₁ - 
epsilon wave.

(N) V₁ = 

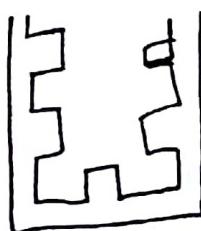
3) X-R

TAZ / Jafazzin

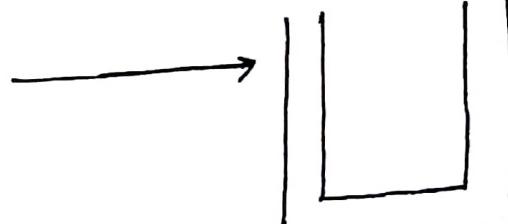
↓
(N) helps in compaction
of ventricle cavity
during embryonic
development

LV non compaction.

* LV thrombus since
birth.



Embryonic



IV Post Myocarditis

80

A Causes :-

1) Infectious

- 1) MC Viral - Coxsackie B
other viral infec"
- Parvovirus B19
- HIV
- Hepatitis C

2) Bacterial

M/c - Diphtheria [death is by myocarditis]

Rx - anti-toxin

3) Protozoa

M/c - Trypanosoma Cruzi
[chaga's Disease]

Rx - Benznidazole

4) Parasite

M/c - Giardimella

Rx - Albendazole

Non-infectious

1) M/c - Sarcoidosis [lung involved]

M/c site → LV free wall

M/c pattern → DCMP > RCMP

Rx = steroids

2) Giant cell Myocarditis

(no lung involvement)

Rx - steroids.

3) Hypersensitivity Myocarditis

cause - Thiazide

Indomethacin

Methyldopa

Rx - cessation of drug
+ steroids

IV. Tako-Tsubo CMP / BROKEN HEART SYNDROME / 81 APICAL BALLOONING SYNDROME

C/F - ♀ + ↑ catecholamine release
↓
vasoconstrictor of LV apex
↓
LV apex non-contractile
↓
During systole RV apex bulge out in systole
like balloon.

Ix - ECG - STT

Thrombin = ↑ or N

coronary angiography → no thrombus

ECHO - LV apex bulging out in systole.



→ Resembles a jar used to trap octopus
↓
hence called Tako-Tsubo.

Rx - reversible, so supportive therapy

+ α blocker followed by β blocker [like phenoxybenzamine]
cytome]

VI . Peri-Partum CMP

Mech:- 1> Autoimmune damage to myocytes by foetal Ag⁸².

2> Prolactin fragments → myocyte damage

C/F:- occurs in 3rd trimester - 6 months post delivery

Risk ↑ → Twin Delivery
multipara
age > 30 yrs

Rx -> Diuretics

2> **Bromocriptine** [by ⊖ Prolactin].

→ also used in Type 2 DM.

RESTRICTIVE CMP

83

Pathology :- Infiltration → Fibrosis

(I) Infiltration

A) In between myocytes

e.g. Amyloidosis

↑ M/CC of RCMP

010

Types

1) **1^o amyloidosis**

Protein/cause

AL / multiple
myeloma

Waldenstrom
macroglobulinemia

NHL

Age - > 50 yrs
M/organ -
Renal

M/CC = CVS
of death

unique - Black eye
Raccoon eye.

Factor Xa adsorb on
AL protein leading to ↑
in blood → blood def. of Xa.
[Ecchymosis]

2) **Familial**

Transthyretin [liver]

↑
genetic

Age > 20 yrs

M/C = CVS

Organ

M/CC of - CVS
death

unique = ascending
neuropathy

1) Liver Transplant

only cond' where liver
Transplantation
is done to out
Liver failure

2)

New Rx

TAFAMIDIS

↳ stabilizes α transthyretin

84

3) Senile
Cardiac
Amyloidosis

Transthyretin
↓ Age.

Age > 70 yrs

M/c organ }
M/c of } CVS
death

Tafamidis

- * 2° amyloidosis doesn't cause restrictive CMP
- * ECG will show low voltage QRS as amyloid is poor conductor
- * Echo = ↑ ventricle wall QRS

(B) Infiltration inside Myocyte.

1) Haemochromatosis

M/c pattern \rightarrow DCMPI > RCMPI
of CMP

M/c of death in untreated pt \rightarrow CVS

M/c of death in treated pt \rightarrow HCC

Rx - Phlebotomy \rightarrow [CMP is reversible]

2) Fabry's Disease

Cause - Defⁿ of α -galactosidase
↓
Glycosphingolipid accumulate

c/F.

85

1) CVS → RCMP

2) Kidney → (GBM damage)

3rd H/c systemic cause of Nephrotic Syndrome

3) Abdomen - Angiokeratoma Q

Rx - Kidney Bx = GBM. \equiv zebra bodies
(electron microscopy)

Rx

Recombinant Galactosidase. [stop the progression of Ds]

(II) Fibrosis

1) Radiation [ca breast/lung] } supportive Rx.

2) Systemic sclerosis

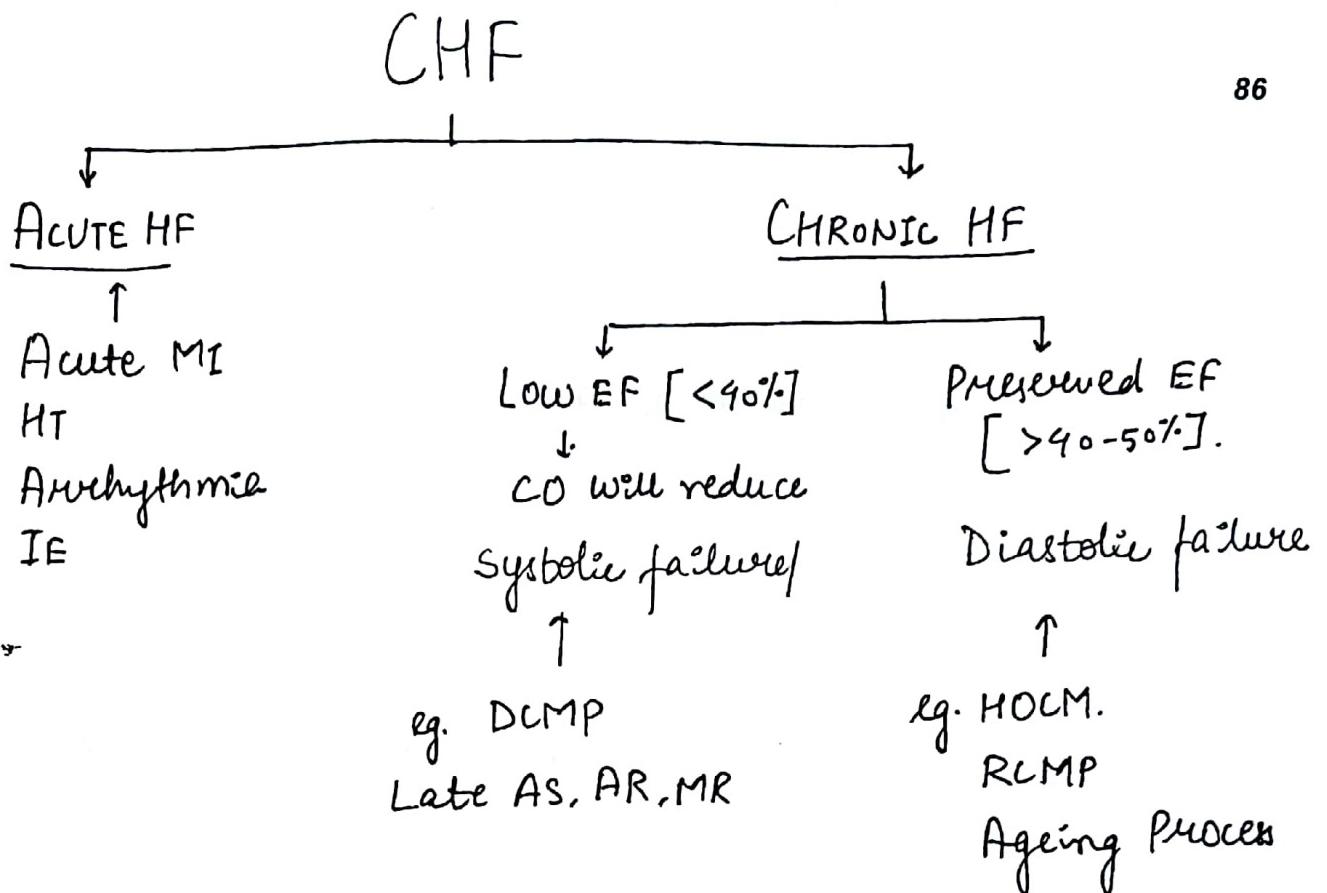
3) Loeffler's Endocarditis

Eosinophilia

Release of ↓ Basic Protein.

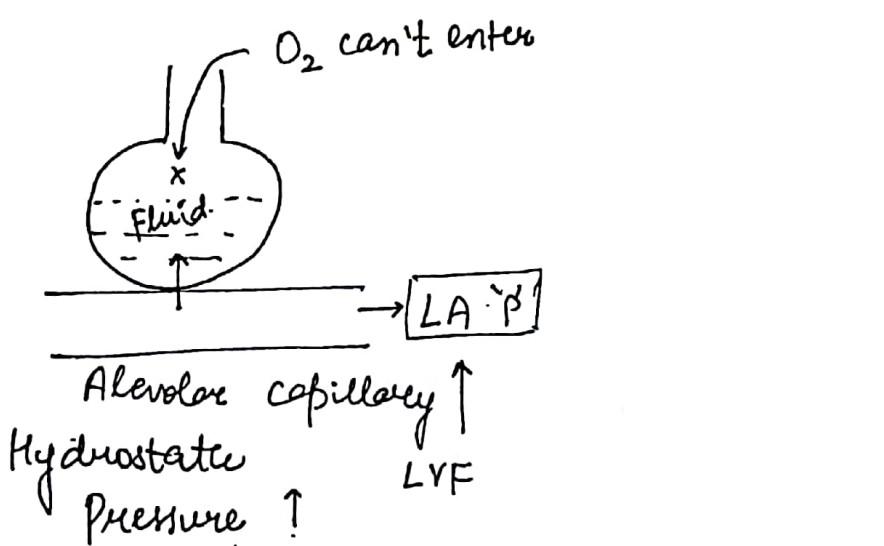
Fibrosis

Rx - Steroid (by ↓ eosinophils)



Rx of Acute HF :-

Acute HF = Acute cardiogenic Pulm. edema



AIM OF Rx - shift alveolar fluid into capillaries
 ↓
 by ↓ capillary hydrostatic pressure
 ↓
 Achieved by ↓ R sided Preload

1> Diuretic [Furosemide]
 +
 2> Morphine [venodilator]
 +
 3> O₂ inhalation.

Initial Rx

87

Systolic BP

<90

Cardiogenic
Shock

[cardiac index
<2.2 L/min/m²
+ SBP <90 for >30 min]

Add - Dobutamine

[slight vasodilator
effect also]

>110.

↓ PCO by ↓
afterload.

Add. Vasodilators

N - Nitroprusside

N - ~~NTG~~ NTG

N - Nesiritide

Add - ↓

DOC - NOR-EPINEPHRINE

Rx of Chv. Heart Failure ⊂ ↓ EF.

↓
Fluid Overload

(+)

(-)

Diuretic

- - - - - → Standard t/t

1> ACE Inhibitors

By ↓ remodelling + ↓ afterload.

a> Metoprolol

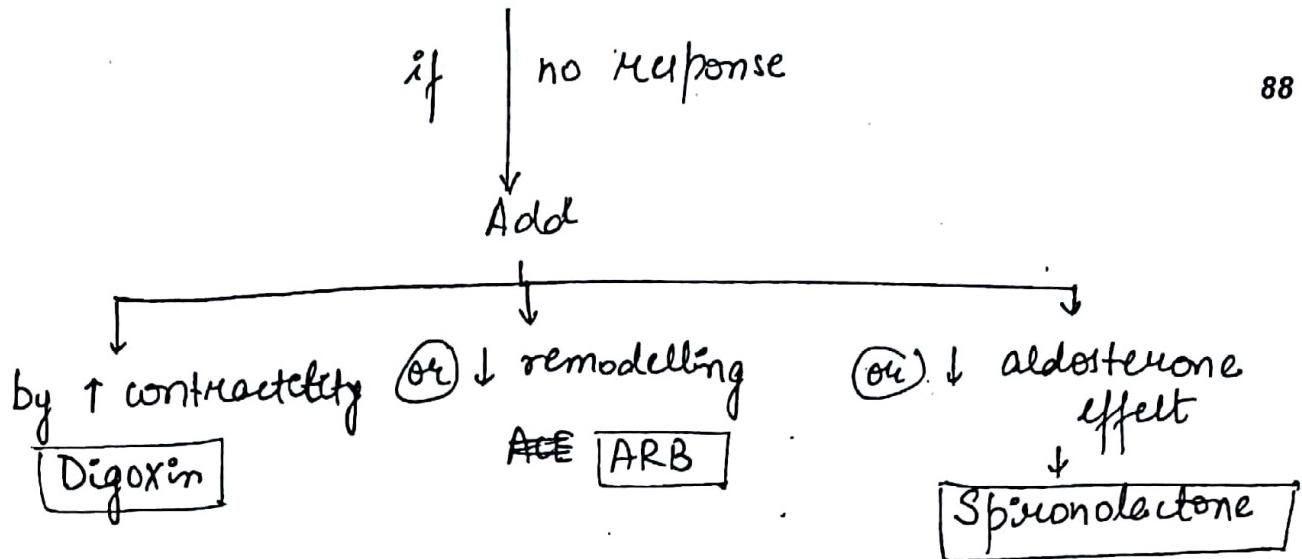
b> Carvedilol

c> Bisoprolol

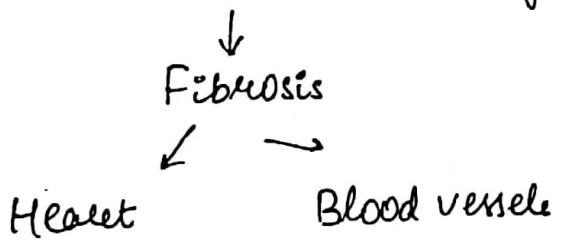
↳ vasodilators also

2> β blocker

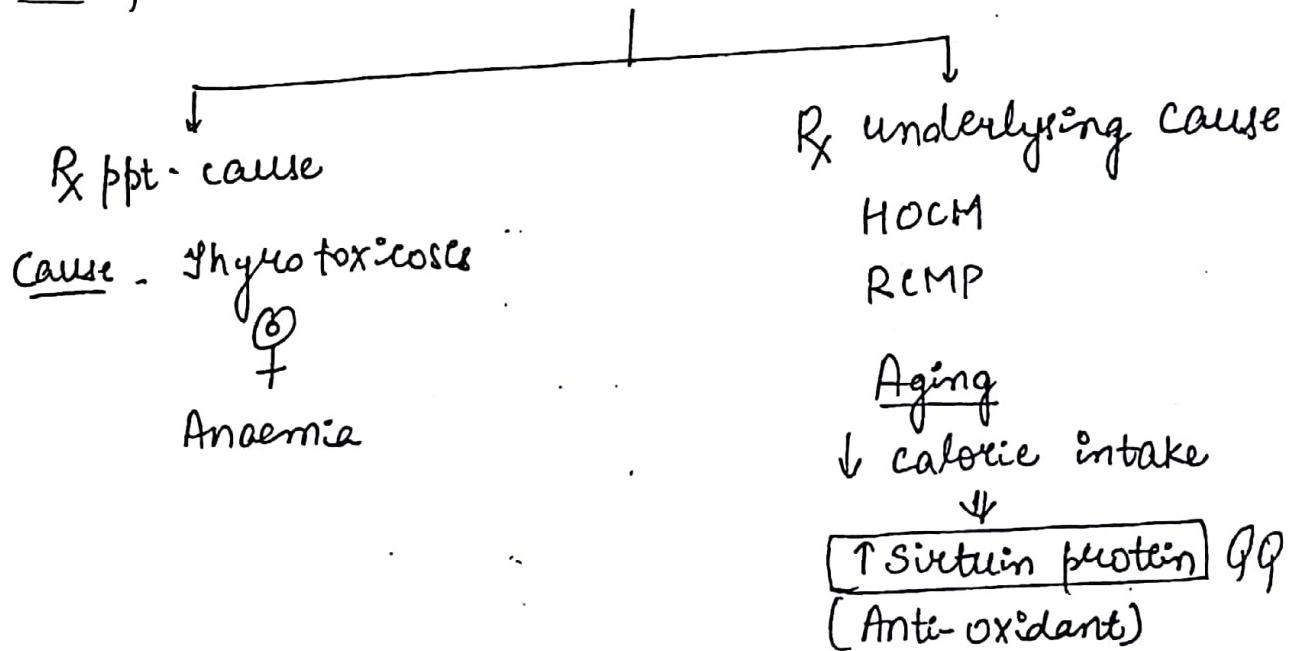
By ↓ workload + ↓ sympathetic activity



Chr. ↓ CO → Chr ↑ aldosterone (by (+)RAAS)



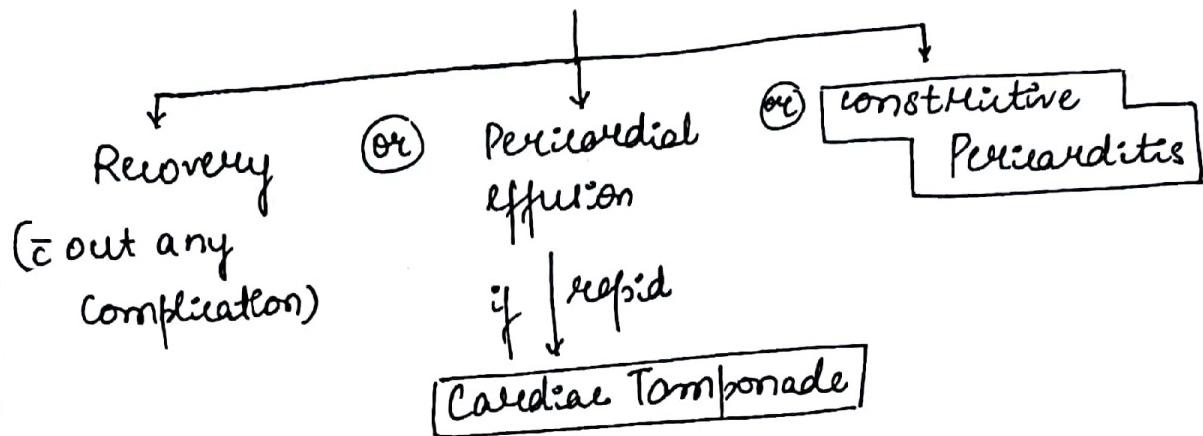
Rx of Chro. HF in Preserved Ejection Fraction



PERICARDIAL DISEASES

89

Acute Pericarditis



ACUTE PERICARDITIS

Cause - H/c - Idiopathic

Symp -
H/c - chest pain [due to rubbing in mediastinal pleura]

Ac. Pericarditis

Site - H/c Retrosternum

Nature - sharp pain

Radiation - Trapezius

Aggravating factors - Supine (as area of contact in pleura ↑)

Relieving - Leaning forward
factor Not relieved by nitrate

Ischaemic Pain

Retrosternum

Dull / constricting

Never sharp

① arm, forearm

Never Radiate to Trapezius

Exertion

Cold Temp

Rest

Sublingual nitrate

Sign - Most Specific \Rightarrow Pericardial Rub.

90

- Crackling sound due to rubbing of 2 inflamed pericardial layers
- Diastolic Phase

I_x

ECG :-



I

PR segment depression +
ST concave upwards ST elevation
[Smiling Phase ST elevation]



II

ST(N) + PR segment (N) or Normal ↓



III

T wave inversion



IV

(N) ECG [Recovery phase]

ECG

91

Ac. Pericarditis

① ST↑ concave upward

② ST↑ all lead.

seen in almost except - ~~other~~
AVR, V₁

③ ST N followed by T inversion

Ac. MI

convex upward.

specific lead

T inversion occur before
T normalize



⊖

⊕

④ trace of reciprocal ST depression in Opp. wall lead

⊖



Deep q Wave

depth > 25% of R wave
+
Duration > 1 mm.

Rx - 1) underlying cause
2) idiopathic:

DOC → NSAIDS

↓ no response

Colchicine

anti-inflammatory +
anti-fibrotic

steroid

no response

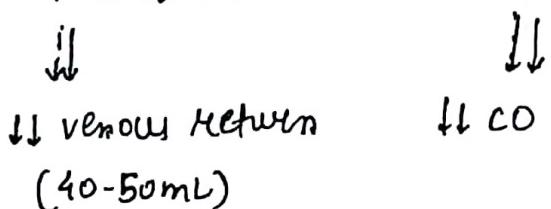
TAMPOONADE

Cause - H/c (world) - idiopathic

H/c in India - TB

Pathophysio - Acute

"Compression" of heart +
venous roots + Aortic roots



Compensatory vigorous
ventricle contract" to
maintain CO.

Obstructive
or shock
Compressive

Symptoms -

H/c → Dyspnoea due to
↓ in resp. H/c
perfusion

* Not due to Pulmonary
congestion.

Lungs - Oliguria

Signs -

Pulse - Pulse Paradoxus
≥ 90% cases

(-) in Tamponade

CONSTRICITIVE PERICARDITIS

92

idiopathic

TB

Chronic

"Failure of relaxation" of
heart due to stiff Pericardium
+ CO is preserved

↓ ↓
↓ venous
return
(100mL)

Compensatory vigorous
ventricle contract"
to maintain CO

H/c → Swelling.

due to ↑ in venous
return.

Hydrostatic 'P' ↑ in systemic
veins

≤ 1/3rd case

Absent Pulm Paradoxus in Tamponade

93

1> AR Tamponade

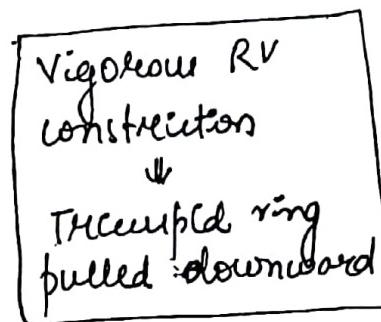
2> CHF

JVP

Deep x

y = Absent

a = Prominent



Deep x

y = Rapid

[failure of relaxation of RA]

Kussmaul = -

(+)

Sign as venous return
doesn't significantly
in Tamponade

Apex - Non-Localised

Non-Localised

soft

S₁/S₂ soft

(-)

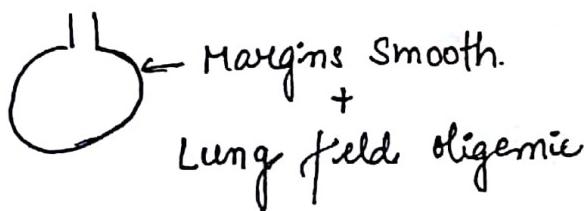
S₃/S₄ (-)

Pericardial knock (+)
[3rd HS]

I_X

① CXR - ↑ cardiac shadow
(Not true cardiomegaly)

CXR - cardiac size normal
+
calcified pericardium



27 ECG =

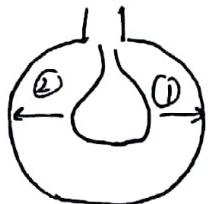
QRS amplitude ↓
[Electric alternans]

ECG

QRS amplitude ↓

94

[Non specific ST ↓ or T ↓]



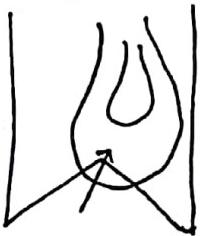
1 ← ECG lead.



Rx

Emergency Pericardacentesis

Routine - Pericardectomy



[ECHO]

Needle [subxiphoid area]

Signs

1) Auenbrugger's Sign

Description

Epigastric Bounding

Bent A

Massive pericardial effusion

2) Beck's Triad

↓ BP + ↑ JVP +
soft HS

Tamponade

3) Ewart's Sign.

compress L side
airway

Massive Pericardial effusion

collapse of distal lungs

↓
Bronchial Breath sound

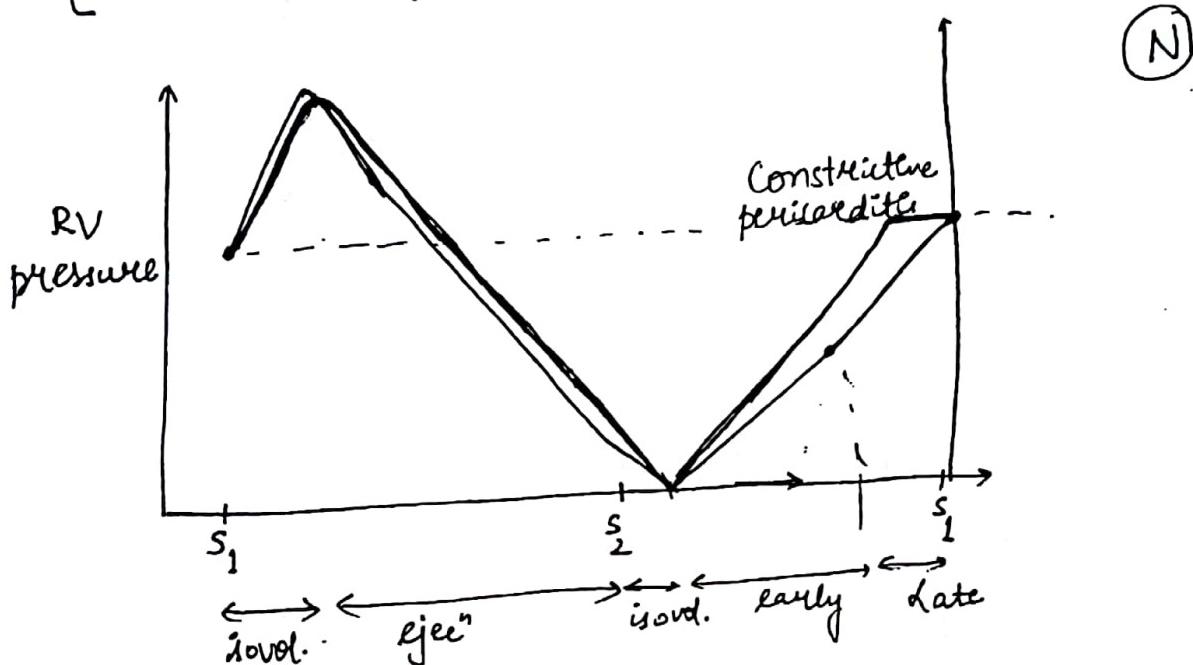
L Infrascapular area

4) Broadbent's sign

systolic retraction of apex
due to fibrous pulling

constrictive pericarditis.

"Square root" sign → constrictive pericarditis.
[Pressure changes in RV]



LMR

SYSTEMIC HTN

96

Classification [AHA guidelines Nov 2017]

	<u>SBP</u>		<u>DBP</u>
1) Normotensive	<120	AND	<80
2) Elevated	120 - 129	AND	<80
3) Stage I HTN	130 - 139	(Or)	80 - 89
4) Stage II HTN	>140	(Or)	>90

Causes

I. Essential / 1° HTN (no identifiable cause)
M/c cause

II. 2° HTN (identifiable cause)



1) M/c 2° cause - Reno-Parenchymal
[cIN, Chr KD].

M/c Mech → vol. overload

2) 2nd M/c → Reno-Vascular
[Renal artery stenosis]

Mech - Ⓛ RAAS

DOC - ACE-I in U/L stenosis

3) Activating Mutation of Sodium channel of tubule.

DCT - Na⁺ channel

Δ GORDEN'S SYNDROME

CD = Ⓛ Na⁺ channel

Δ - Liddle's Syndrome

DOC - Thiazide

DOC = Amiloride.

97

4). Endocrine causes.

Endocrine

a) Hypothyroid

Type of HT

DBP ↑

(compress bld. vessels)

Edema

(+)

Myxoedema

Conn's Syndrome

DBP ↑

(-)

b) Chr. ↑ aldosterone
↳ vessels fibrosis

ANP released

↓

"Escape" Mechanism

c) Hyperthyroidism

SBP ↑

(due to ↑ CO)

(-)

d) Phaeochromocytoma

SBP + DBP ↑

(-)

sustained HT > episodic HT

5). Miscellaneous causes

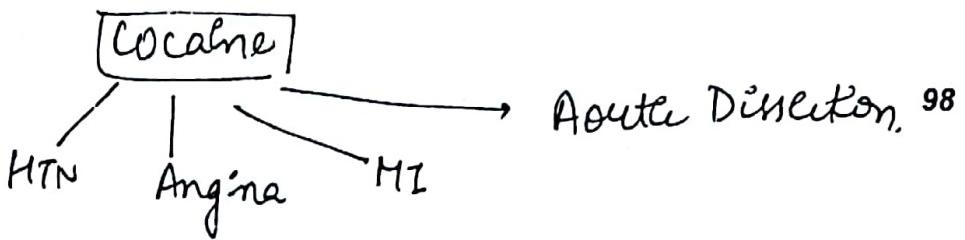
a) M/c long. CV cause of HTN ⇒ Coarctation of Aorta

b) Systemic HTN ← sympathetic ↑ ⇒ Obstructive sleep Apnoea

Pulm. HTN ← hypoxia

c) PCOD = Insulin resistance
[acanthosis nigra]

d) Drug NSAIDS by ↓ GFR
Corticoesteroid
estrogen



Symptom

1) M/c - Dyspnoea [due to CHF]

$$\text{M/c of CHF} = \boxed{\text{HTN}}$$

2) M/c symp due to HTN → Occipital Headache

3) Sign → LVS₄ + (due to LVH)

I_x -

ECG changes

1) LVH signs

2) LA enlargement

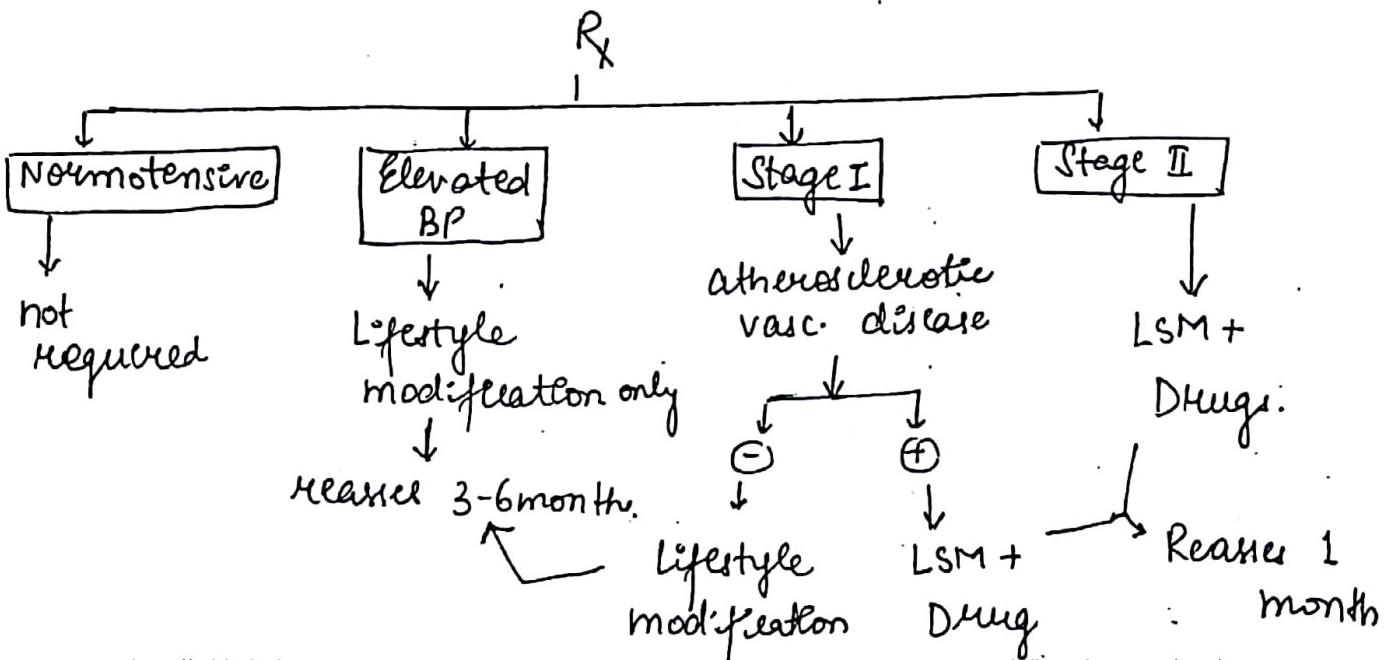
3) LAD

Rx

Stable

≥ 2 readings on ≥ 2 occasions

should be ↑ to Δ HTN



* Lifestyle Modification

99

- 1) wt. Reduce
- 2) $\downarrow \text{Na} \leq 1.5 \text{ gm/day}$
- 3) $\uparrow \text{K} 3.5-5 \text{ gm/day}$ cause smooth M/s relaxation
- 4) **DASH DIET**

Dietary Action To Stop HTN

$\downarrow \text{Na}^+$ \downarrow Fat dairy product,
 \uparrow Fruits + veg., \downarrow saturated fat

5) Break Walk / Exercise $\geq 150 \text{ min/wk}$

6) Alcohol $\text{♂} < 30 \text{ g/d}$ $\text{♀} < 15 \text{ g/d}$

Other Terms

1) Resistant HTN
if $\text{BP} \geq \frac{140}{90}$ despite ≥ 3 drug (one of ≤ 2 diabetic)
or

if $\text{BP} < \frac{140}{90}$ $\cong \geq 4$ drug

M/CC \rightarrow Non-compliance

2) White Coat HTN

In clinic if $\text{SBP} > 20$ or $\text{DBP} > 10$ from non denoted readings.

3) HTN Emergency = If $\boxed{\text{BP} > 180/120}$ \cong Target Organ Damage

I.v. Labetalol $\leftarrow 1\right)$ Haemorrhage Stroke

I.v. ~~Nitro~~ NTG or Nifedipine $\leftarrow 2\right)$ Ac. cardiogenic Pulm. Oedema

I.v. NTG $\leftarrow 3\right)$ Ac. MI

I.v. Esmolol $\leftarrow 4\right)$ Aortic Dissecⁿ

Nimodipine $\leftarrow 5\right)$ SAH

* Mean BP reduction → 25% from presentation value
$$\left[DBP + \frac{1}{3} PP \right] < 1-2 \text{ hrs.}$$
 100

* DOC for HT Emergency = I.V. Nicardipine

* 4) HTN Urgency = $\frac{BP > 160}{120}$ + no target organ damage

Rx = combination of oral drugs.
[OPD]

5) Orthostatic Hypotension

if SBP ↓ by > 20] in 3 min of standing

DBP ↓ by > 10

M/c cause → Hypovolemia

2° HTN associated with
orthostatic HTN

= Phaeochromocytoma

Chr. vol. depleted.

↑

due to Chr. vasoconstrict.

IHD

101

Stable Angina

Unstable Angina

Non-ST ↑
MI
(Subendocardial)

ST ↑
MI
[Transmural]

20-30 min

> 30 min

Duration
= 2-10 min

20 min

⊕

⊕

Pain at rest

⊕

ECG at rest

N

ST depression
[except Prinzmetal
Angina]

ST depression

ST elevation.

Trophonins

N

N

-↑

↑

Symptoms

M/c → chest pain

Painless MI → Autonomic Dysfunction
[DM, elderly]



'Angina' equivalent symptoms

a) Unexplained sweating

b) " Dyspnoea

c) Sense of impending Doom

Signs M/c → LEVIN SIGN [Holding Palm or Fist against
retrosternum]

Pulse - if tachycardia = Ant. wall

Bradycardia = Inf. wall

JVP - if Kussmaul sign = RV MI.

S₂ = if split is wide = RVMI [late P₂]
 if split is reversed = LVMI [late A₂]

102

poor prognosis S₃ - if + → indicate systolic failure
 [Infarct > 40%]

S₄ - +

[more common than S₃]

Murmurs -

Papillary M/s Necrosis

Acute MR

early Systolic

Septal Rupture of ventricle

VSD

Pansystolic

I_x ① ECG

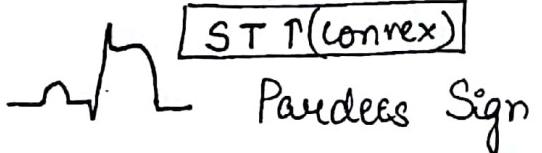
Sequence of changes

1>



(> 50% of R wave height)

2>



3>



Mech

Leakage of K⁺

[Similar to hyperkalemia]

Early Repolarisation of infarcted m/s

Non-specific

4)

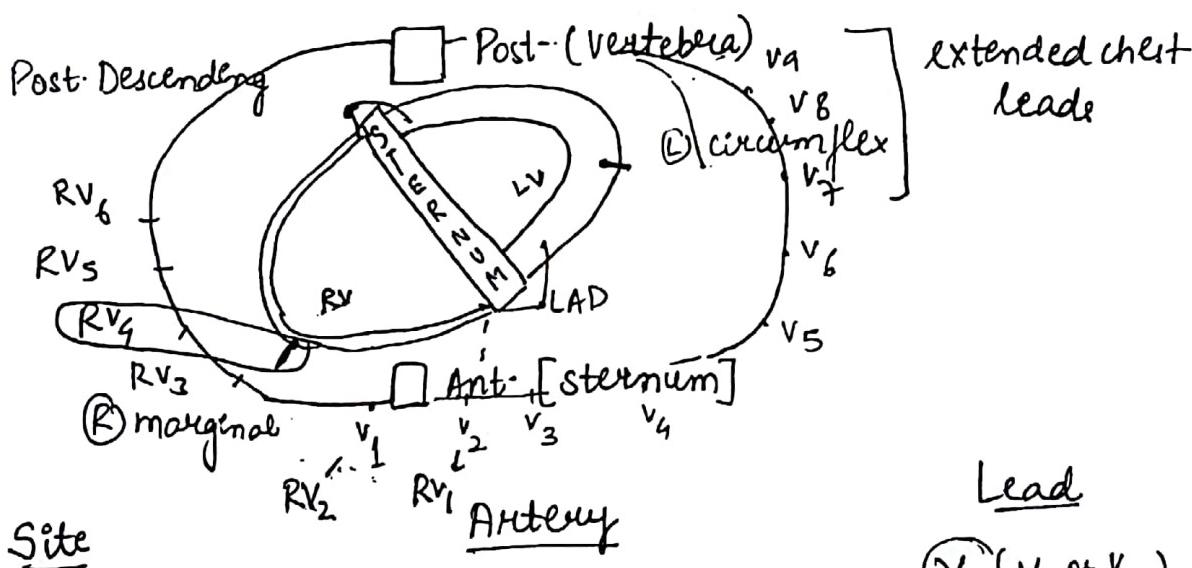
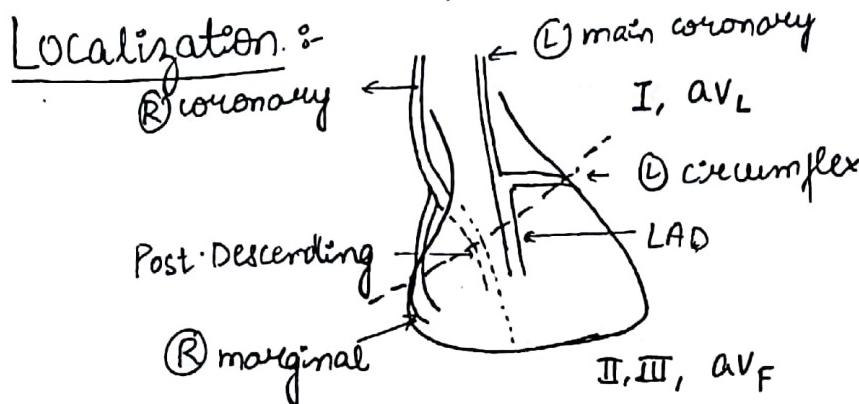


Pathological Q wave

Necrosis

103

NO use of thrombolytic therapy



V₇ - V₉ - ST ↑
or

V₁ - V₉ → reciprocal ST ↓

RV₄

⑥ Inf wall

⑧ coronary via post
descending

II, III, aVF
₁₀₄

⑦ Antero-Lateral
MI

⑨ main coronary

V₁ - V₆, I, aVL

$$RxOc = CABG \text{ (not PCI)}$$

not ~~far~~ flexible

⑩ Cardiac F
Markers

Time to ↑ in blood
(after symptoms)

Time to N

1) Heart Type FA
Binding Protein

2 hrs

24 hrs

2) Myoglobin

3 hrs

24 hrs

3) Troponin I [Best]
T

6 hrs

10-14 days

4) CPK-MB

6 hrs

72 hrs

→ Preferred over Troponin of re-infarct 3-10 days

Troponin can be used in re-infarct.

if >20% ↑ from baseline

Rx (I) ST ↑ MI

105

Initial Rx

Role

1> **Aspirin** [non-enteric coated] Essential in all
Dose - 325mg chewable

if O₂ saturation is ↓

2> **O₂ inhalation**

Analgesic

3> **I.V. Morphine**

+
Ac. cardiogenic Pulmonary edema

4>

C/I in **RVMI**

[↓ Preload → further ↓ CO]

4>

Nitrate

coronary vasodilatation.

+
↑ BPT

C/I - **RVMI**

5>

β blocker
metofenadol

↓ workload

C/I - Asthma

PR interval > 0.25 sec

6>

ACEI

All pts. for initial 48 hours

↓
continue if HT (+)

7> **High Dose Statins**

Anti-inflammatory +

Atorva 80mg/d.

Plaque stabilizing Property.

8> **Clopidogrel**

300mg loading Dose

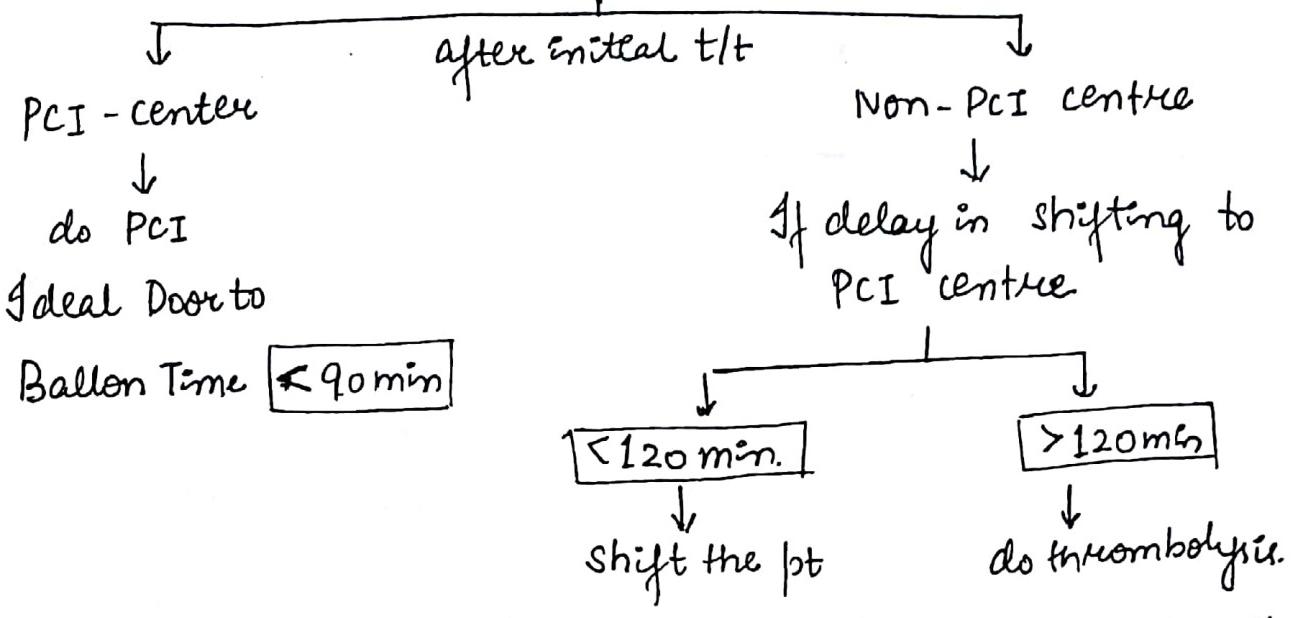
of pt undergoing procedure

PCI.

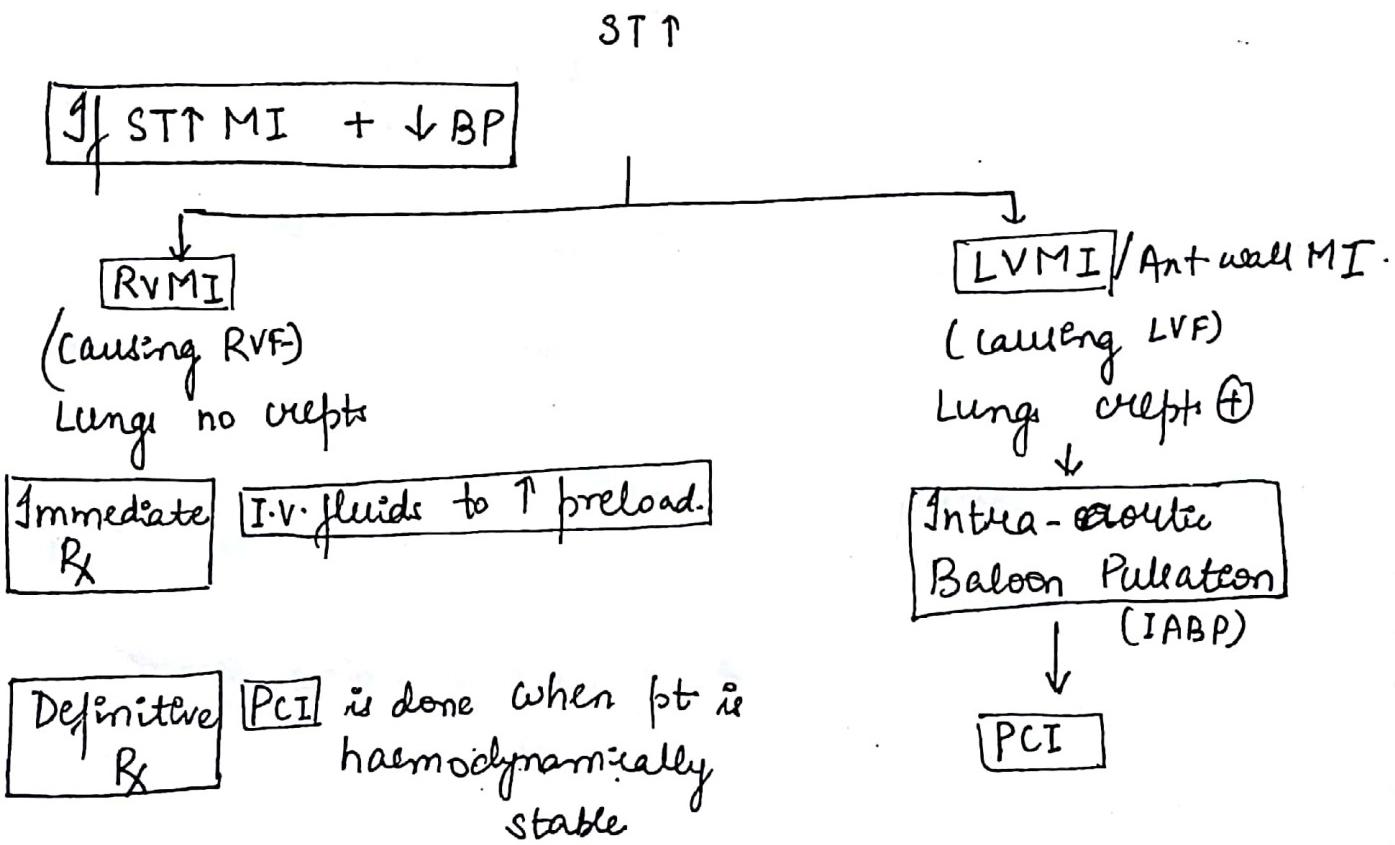
Definitive Rx = PCI > Thrombolysis

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If ST↑ MI Presented to



If symptom < 12 hours duration.
+ ST↑



Rx (II) Non-ST ↑ MI / Unstable Angina

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Std. Rx

1) Anti-platelets = aspirin + dabigatran

+

2) Anti-thrombotic agents. = LMWH or Thrombin (-)

+

③ Nitrate

+

④ β blocker

↓ if there is no relief

Add CCB

↓ if no relief

PCI

(III) Stable Angina

↳ Aspirin Life long

↳ Sublingual dinitrate

↳ Rx risk factors

PRINZMETAL ANGINA

Cause - Idiopathic vasospasm of epicardial coronary artery. [non-atherosclerotic]

M/c artery affected → (R) Coronary

C/F -

↳ Smoker + young age

* Associated symptoms = Raynaud's phenomenon

* Pain = 12 AM to 8 AM.

I_x - ECG - ST ↑
Thiopronin = N

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- R_x -
- 1) Acute → vasodilators = Nitrate → CCB α-Blocker
 - 2) Maintenance → CCB
 - 3) C/I → Aspirin
β Blocker → ⊖/Lower vasodilator PG_I
→ ↓ pt. vasoconstriction

Q. In intraoperative MI ⊂ drug not used.

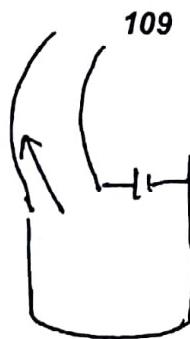
- Ⓐ Heparin → Best ECG Lead V₅ or V₄
- Ⓑ Atropine if AV Block
- Ⓒ CCB
- Ⓓ NTG.

LMP.

AORTIC DISSECTION

[causes -

- 1) M/c → HTN M/c site → ascending aorta (R)
Lateral wall
- 2)
- 3) Large vessel vasculitis
Takayasu
Giant cell arteritis.
- 4) Drug - cocaine
- 5) ♂



Types

A/c to Site of Origin [Stanford classification]

(A)

Ascending aorta
more common
more fatal

(B)

Descending aorta

A/c to Extension [DeBakey classification]

I

II

III A

III B

to descending aorta also

Limited to ascending aorta

Above diaphragm

Below diaphragm.

Symptom M/c - chest pain

Retrosternal + Tearing Pain + Radiation to intercapsular area¹¹⁰

Sign Asymmetrical Pulses

Acute Aortic Regurgitation. [due to type A dissec]

Ix

1) CXR → Wide mediastinum

+
① Sided Pleural effusion (20%)

↓
D/D of Oesophageal Rupture

↓
H/o vomiting

2) Unstable pt. → Trans oesophageal ECHO.

3) If pt. is stable → CT

4) Gold Std. Ix → MR angio

Rx

Initial Rx → BP

High or N

Low

(Target SBP 100-120 mm Hg)

I.V. fluid.

I.V. ESMOLOL

Definitive Rx

Type

↓
A

Urgent surgical
Repair.

↓

B

Conservative

do surgery if

- * Impending rupture
- * Limb / Visceral ischaemia

RHEUMATOLOGY

IMMUNE SYSTEM

115

INNATE

- 1) ANATOMICAL BARRIER
- 2) PRR's (pattern Recognizing Receptors)
Inflammasome Proteins (Sensors)
- 3) Anti-Microbial Peptides (AMPs)
Lysozymes - Tears/Saliva

4) NK cells (BOUNCERS)

Largest WBC

Regulated by T cells (IL-2)

Immune + Tumour surveillance

Non-immune mediated action

Only immune cell → non-MHC
restricted action.

(virus infected / mutated cells
are also checked by these cells)

5) MONOCYTE - MACROPHAGE SYSTEM (Police)

6) Dendritic cells (Most Potent APC's)

7) GRANULOCYTE SERIES (N, B, E)

8) COMPLEMENT CASCADE. Regulators of immune response

a) CYTOKINE

ADAPTIVE

1) B cells (HUMORAL)

- express CD_{19,20} on surface
- when activated

PLASMA CELLS

↓ Immunoglobulins (antibodies)

2) T cells (cell mediated)

- CD₄ " CD₈
(Helper) (cytotoxic)
Most Potent level of
immunity

IMMUNE EXCESS DISORDERS

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INNATE (AUTOINFLAMMATORY)

FAMILIAL MEDITERRANEAN FEVER (FMF)

(Recurrent Poly-Serofitis)*

EPID - 10-20 yrs, ♂>♀

ETIOPATH - Inherited defect of MEFV gene

Overexpression of the PRR's
INNATE EXCESS STATE

C/F → Recurrent Febrile Illness
(each last for 6-8 weeks)

constitutional symp :- Anorexia
wt. loss
myalgia

HL ↓			
Pleuritis	Peritonitis	Arthritis	Pericarditis
D/D - TB	D/D - Appendicitis	D/D Juvenile RA	D/D Rheumatic fever

A :- Clinical suspicion → GS (Genetic testing MEFV gene)

Rx :- COLCHICIN - Favourable response + longterm remission.

Dreaded complication :- 2° Amyloidosis - Nephrotic syndrome
High Mortality

Recurrent Febrile Illness → Unconfirmed Infection
= Rheumatology

ADAPTIVE AUTOIMMUNE DISORDER

ORGAN SPECIFIC

Myasthenia Gravis

Graue's

Pernicious Anaemia

SYSTEMIC

= RHEUMATOLOGY

Study of systemic autoimmune disorders.

ANTIBODY TESTING

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INDEX

LUPUS group
(Skin rash)
"wolf-Bite"

- 1) SLE
- 2) Systemic sclerosis
- 3) Sjogrens (sicca)
- 4) M.C.T.D.
- 5) Rheumatoid

ARTHRITIS
Approach.

- 1) RA
- 2) Spondylo arthropathy
- 3) Crystal induced
- 4) CHARCOT's joint (neuropathic)

VASCULITIS

- 1) Misc. Pain syndrome
 - fibromyalgia
 - chronic fatigue syndrome

ANTIBODY

ANA

CLINICAL SIGNIFICANCE (Best Screening)

M/c Ig found in autoimmune disorders
(>98% of case)

MOST SENSITIVE Ig

ELISA

METHODS → IF (Preferred)

Qualitative Result (+/-)
Hence it is non specific

- 1) Quantitative (Result in titres)
 - <1:160 = + in 20% Healthy population
 - >1:160 = SIGNIFICANT (More specific)
- 2) IF PATTERN (due to the A)

IF PATTERN

M/c - SPECKLED

Homogenous

Rim pattern

Centromere

Nuclear Pattern

ANTIBODY

Anti-Ro/La [SSA/SSB]

Anti-dsDNA - M/c in SLE

Anti-smith - Most specific for SLE

Anti-centromere (specific)

Anti-topoisomerase-1 (SCL-70 commercial)

DIAGNOSIS

SICCA SYNDROME.

} SLE

→ Localised Systemic Sclerosis

→ Systemic sclerosis

ANTIBODY

Anti-Sm
(not preferred)

Anti-dsDNA
(preferred)

APLA
(phospholipid)

Anti-Histone
(specific for
Drug induced
SLE)

CLINICAL SIGNIFICANCE

(Astie Role
in SLE)

MOST SPECIFIC for SLE
Only in 10% (lacks sensitivity)
NO correlation \cong disease activity

② Sensitive + Specific
correlates \cong disease severity
Associated \cong \uparrow Risk - nephritis/CNS involvement.

Present in 60-70% cases of SLE
Associated \cong vascular thrombosis (fetal Loss)
Most recent to be ~~included~~ included in
Δ criteria of SLE.

CVS	^{HIC}	ACEI, β blockers, Thiazides, Statins Methyldopa, Hydralazine, Procainamide
-----	----------------	---

Anti-microbial	INH, Dapsone, Sulfonamides
----------------	----------------------------

CNS	Phenytoin, carbamazepine
-----	--------------------------

GIT	Sulfasalazine,
-----	----------------

Endo	Propylthiouracil
------	------------------

Misc	d-penicillamine
------	-----------------

New	Interferons Anti-TNF α
-----	----------------------------------

ANTIBODY	CLINICAL SIGNIFICANCE. (Prognostic Role)	
Anti-Ro/La Crosses placenta	↑ Risk of congenital Lupus ↓ Risk of maternal Nephritis	SSA/SSB Astro Role in sicca syndrome
Anti- Ribosomal P	↑ Neuro-psychiatric convulsion + Psychosis	↑ Risk of CNS Lupus
Anti- Neuronal Ab	↑ Neuropathy R. Painful, Axonal	
Anti- erythrocyte	Hemolytic anaemia	↑ Risk of hematological involvement
Anti- platelet	Thrombocytopenia	

ANTIBODY	CLINICAL SIGNIFICANCE	
Anti- centromere	Localised Scleroderma (CREST syndrome)	Astro Role in ssc
Anti- SCL70	Diffuse ssc	
Anti- U ₃ RNP	↑ Risk of PAH + RPGN	Prognostic Role in ssc.
Anti- U1RNP	specific for Mixed connective Tissue Disorder	
Rheumatoid factor (RAF) IgM Ig against Fc portion of IgG	Best screening Test for RA (PROT. SENSITIVE) Correlate - Risk Bone erosions (PROGNOSIS) Non-specific for A	

ACPA / Anti- CCP
(Most specific
for R.A.)

Anti-cyclic citrullinated Protein Ab.
(Aster Role in RA) 121

ANCA
(anti-neutrophil
cytoplasmic Ag)

Vasculitis (Aster Role)

cANCA
Anti- PR3
(proteinase-3)

pANCA
Anti- MPO
(myeloperoxidase)

SLE

M/c autoimmune disorder

Epid - 20-40 yrs. ♀ > ♂

Cause - Idiopathic M/c

- Risk factors -
- 1) GENETIC - TREX-1 gene defect
 - 2) CHROMOSOMAL - Klinefelter's syn.
 - 3) INFECTIONS - EBV
 - 4) TOXINS - UV Rays, Silicosis

Manifestation

Clinical Description.

1) Cutaneous

a) Acute :- MALAR RASH

b) Chronic :- DISCOID RASH

2) Oral ulcers

excluding - a) nutritional b) infective

c) Behcet's disease

Considered as

SLE

3) Alopecia

excluding - a) Nutritional (Iron, Zn)

(considered as SLE)

b) Endocrine - thyroiditis (Hypo)

c) Drug induced

4) Synovitis (90%)
(Non erosive
arthritis)

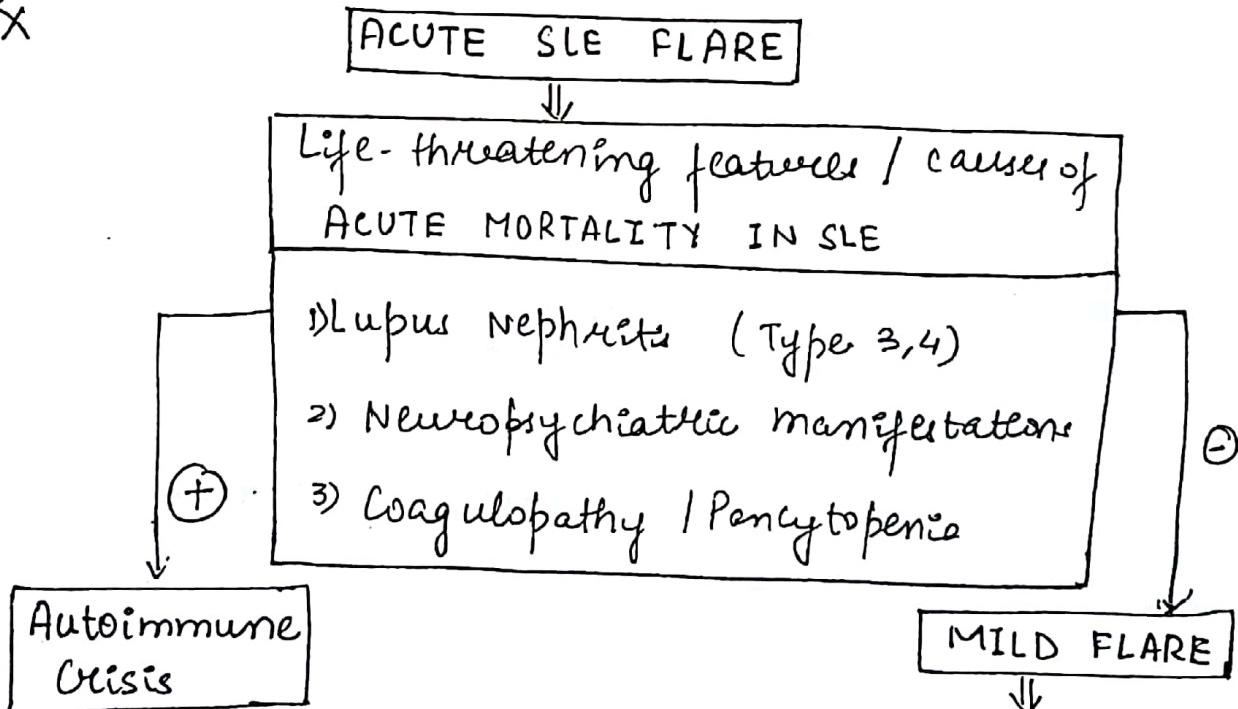
M/c Symmetrical polyarthriti
NEVER DEFORMITY / Bone Disease

5) RENAL	Proteinuria $> 3+$, Granular/RBC cast	122
6) CNS	Neuropsy., Neuropathy	
7) ANAEMIA	Hemolytic - Hb $\leq 10\text{ g/dL}$	
8) LEUCOPENIA	WBC ≤ 4000 or Lympho ≤ 1000	
9) Thrombocytopenia	Platelet $\leq 1,00,000$	

Δ :- SLICC Criteria (Systemic Lupus International Collaborative Clinics)

9 clinical ABOVE manifestations	6 Immunological.	≥ 4 confirms SLE (at least 1 of each)
	1) ANCA ② AnticSm 3) Anti Ds DNA	④ APLA ⑤ Direct Coombs Test +ve ⑥ Low serum C3 Level

Rx



Rx : IV Methyl Prednisolone **PULSE** → Oral Prednisolone
 $1\text{ gm/day} = 3-5 \text{ days}$

(Lifetime)

$1-2\text{ mg/kg/day}$
 ↓
 Add steroid sparing
 MYCOPHENOLATE MOFETI

Approved alternatives to methylprednisolone

123

RITUXIMAB (Mab \ominus CD₂₀)

BELIMUMAB (Mab \ominus BAF)

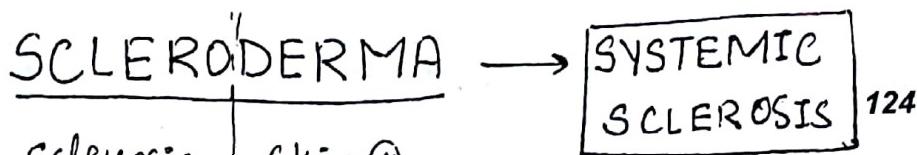
POOR PROGNOSIS

Affects Productive age group	unpredictable course of the disease	High cost of therapy	Long Term Adverse drug Rxn of immuno suppression	NO CURE (lifelong therapy)
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ACUTE ← MORTALITY IN SLE.

↓
CHRONIC/ Longterm

- 1) Thrombotic events - cardiac failure
- 2) Opportunistic Disease



>98% have systemic involvement.

epid - 30-50 yrs, ♀ > ♂

cause - H/c - idiopathic

Risk factors → 1) INFECTION → CMV, Parv B19

2) TOXIN EXPOSURE - Scleroderma, "Toxic Oil Syndrome"

C/F \downarrow H/c

1) RAYNAUD's → can precede skin changes ≥ 10 yrs



2) SKIN changes : Hands + face

	HANDS	FACE
a) DEDAMATOUS	Puffiness of finger	Face
b) INDURATIVE	claw hand deformity	Mask-like
c) SCLEROSIS (most specific) (HOST SPECIFIC)	Autoresorp of terminal phalanx ↓ shortening of digits	"FISH-MOUTH" appearance

CLASSIFICATION - Based on Extent of skin involvement

ONLY SKIN (<2% cases)	Restricted to face	Proximal - elbow	only organ.
MORPHIA	Distal to elbow	Trunk +	SCLERODERMA
En-coup-de-sabre Lesion	↓ Localised	↓ Diffuse	SINE SYNDROME (Least common)
sickle	SSC		

Suspected →

SSc

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Face & Distal to elbow

LOCALISED SSc

Anti-Centromere \oplus

Proximal to elbow

DIFFUSE SSc

SCL-70 / Topoisomerase - 1 Ab \oplus



'CREST'

Also called

✓ Calcinosis

✓ Raynaud's (Doc = CCB)

✓ Esoph. dysmotility (GERD)

✓ Telangiectasia \xrightarrow{s} sclerodactyly

Above features are M/c E

Localised >> Diffuse



More risk of organ involvement

Lung: - M/c type of ILD in autoimmune disorder

NSIP (non-specific interstitial
↳ Doc - Steroids + pneumonia)

↳ Pulmonary artery HTN

(Doc - Sildenafil)

RPGN

(Renal crisis) (Doc - Captopril)

Rx = ONLY PALLIATIVE

NO CURE

Unfavourable Prognosis

SICCA SYNDROME

(Sjogren's Syndrome)

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M/c manifestation - Dryness of Eyes & Mouth.

Lymphocytic infiltration of exocrine glands

CAUSES

1° SICCA (Idiopathic) Rate

[SICCA - is the Disease]

- High Risk → Systemic (extraglandular manifestations)
- High titres → SSA/SSB Ab
- High Risk → LYMPHOMA (M/e of death in SICCA)
- Majority → Immunosuppressants.
- POOR PROGNOSIS

M/c

2° SICCA

[Underlying disease]

- SLE, SSC, MCTD, RA, vasculitis
- 1° Biliary Cirrhosis
- chr. autoimmune Hepatitis
- only Glandular symptoms
- Low titres - SSA/SSB
- NO risk of Lymphoma
- Rx - only palliative
FAVOURABLE PROGNOSIS

C/F

GLANDULAR.

SYSTEMIC

Involved	C/F	TEST	Rx	
Lacrimal Gland	Dry-eye	Schirmer	Artificial tears	<p>LUNGS - M/c - NScf</p> <p>Isolated PAH</p> <p>Renal - (M/c)</p> <p>Distal RTA -</p> <p>- Interstitial nephritis</p> <p>Liver - Cirrhosis</p> <p>CNS - neuropathy</p>
	corneal or conjunctival erosions	Rose Bengal Test	Protective glasses	
Salivary	Dry-mouth	Gonto pho-Mesg	Hydration	
Pancreas	Hab's syndrome	Stool FAT estimation	Enzyme replacement	LYMPHOMA - most dreaded

Rx 2° SICCA → only palliative

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1° SICCA → Depends on organ involvement

GOOD PROGNOSIS (majority are 2°)

POOR PROGNOSTIC FACTORS

- 1) Elderly onset (>40). ♀
- 2) B/L parotid enlarged
- 3) Systemic +
- 4) High titres of SSA/SSB.

OVERLAP SYNDROMES

Epid = 10-20 yrs, ♀ >> ♂

C/F = (SLE/ SSC/ SICCA) + (R.A.)

Screening = ↓ ↓
Ab ANA RAF
 +ve +ve

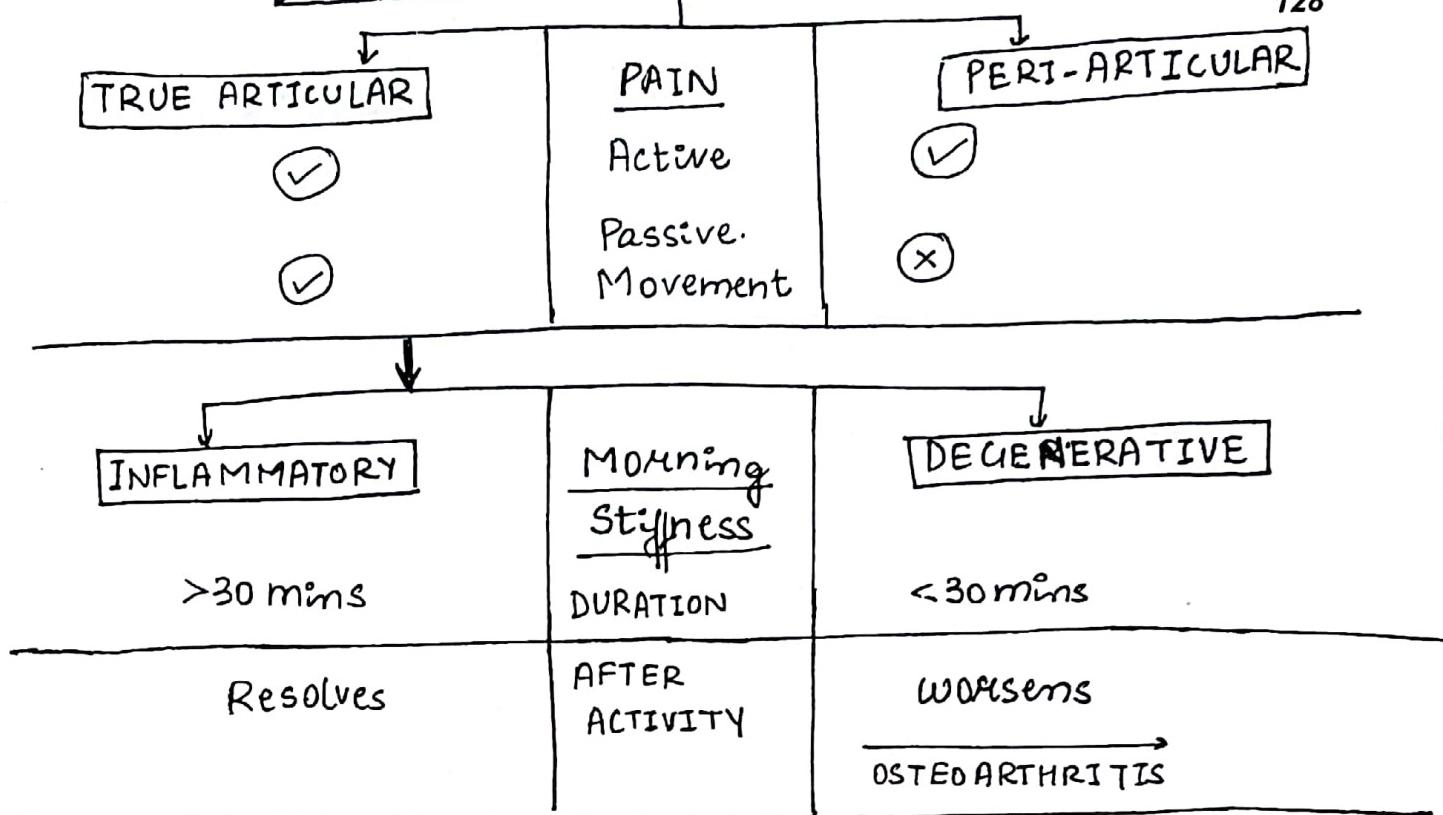


Rx		SLE Dominant	RA Dominant
Immuno suppression		DMARDs	
Non-erosive arthritis		Erosive arthritis	

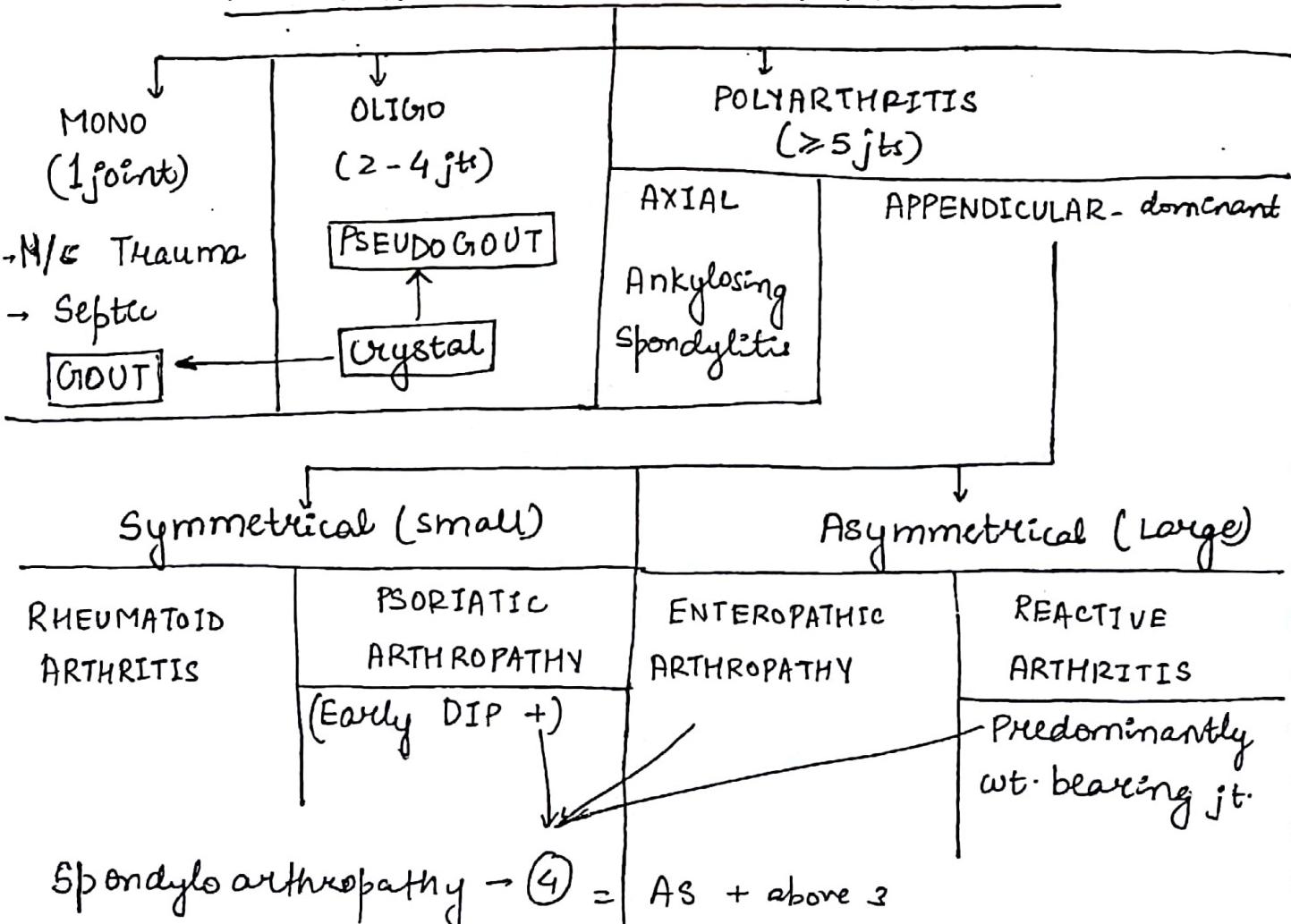
PROGNOSIS - Better than individual disease
Better response to therapy

APPROACH TO JOINT DISORDERS

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APPROACH TO INFLAMMATORY ARTHRITIS



MIC Pattern of Joint Involvement in Diseases

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↓
Most Imp parameter for Diagnosis of arthritis

RHEUMATOID ARTHRITIS

Epid- 30,50 yrs, ♀ > ♂

H/c - Idiopathic

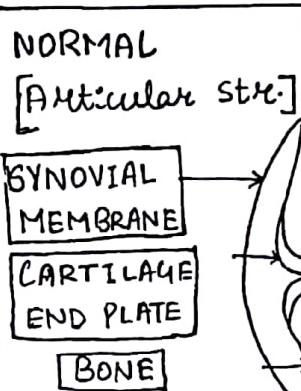
Risk Factors - 1) GENETIC = **HLA-DR4** (Most cases = sporadic)
2) INFECTION = **Mycoplasma, EBV**

C/F

ARTICULAR (predominant)

EXTRA-ARTICULAR

- Inflammatory Poly-arthritides
- Appendicular Dominant
- Spine involvement - Rare
 - ↳ H/c - Atlanto-axial jt.
- Symmetrical, small jts. of hand
Wrist, MCP jt + PIP jt



- STAGE-RA
- 1) SYNOVITIS
 - 2) PANNUS FORMATION
 - 3) BONE EROSION
 - ↓
Jt. Destrucn
 - Jt. Deformity
(irreversible stage
of Disease)

EPISCLERITIS

LUNG | H/c usual Interstitial Pneumonia (UIP)
H/c → ♂

Pleuroperitoneal

Valvular H/c → MR

MUSCULO-SKELETAL

↓ Myopathy ↓ Osteopenia
Fast progress - OA

FELTY's (RA + spleen)

↓
Anæmia / Neutropenia
Risk of Lymphoma
Least common
≤ 1% - advanced RA
Early DMARD Rx

Δ :- EULAR (European League against Rheumatism)
Guidelines - A scoring system 130

(A) PATTERN of joint involvement (Max : 5)

- 1 jt (Predom- Large) → 0
- 2-10 jts → 1
- 1-3 jts → 2
- 4-10 jts (Predom- small) → 3
- > 10 jts → 5

(B) SEROLOGY (Both RAF + ACPA) [Max = 3]

NEGATIVE → 0

MILD \oplus [$< 3 \times$ upper
normal
limit] → 2

STRONG \oplus [$> 3 \times$ upper limit] → 3

(C) DURATION

- | | |
|-------------|--|
| < 6 wks - 0 | |
| > 6 wks - 1 | |

(D) ACUTE PHASE REACTANT

NEGATIVE → 0

ELEVATED → 1

Δ = ≥ 6 confirms RA.

RADIOLOGY \otimes → Not recommended for Asse.

OLD CRITERIA :-	X-Ray Hand ↓ X-Ray - Least sensitive test MRI - MOST SENSITIVE test ↓ Impractical	= Bone Erosions ↓ Late, irreversible stage Earliest feature of RA Juxta-articular osteopenia ↓ NON-SPECIFIC.
-----------------	---	--

Rx Most preferred method → STAGE the severity

CDAI (Clinical Disease Activity Index)

2.8 - 10	10 - 22	> 22
MILD RA	MODERATE RA	SEVERE RA
Single DMARD	COMBINATION DMARD	Early use of Biologicals

Prognosis :- Favourable → **REMISSION** → can be achieved in 60-85% cases

POOR PROGNOSTIC FACTORS :-

- 1) Elderly (> 60)
- 2) ♀
- 3) > 10 yrs @ onset
- 4) High titres of RRF
- 5) Delay in initiation of DMARD ≥ 3 months

DMARDs	InD ⁿ	ADR	Follow-up
METHOTREXATE (MTx)	1st choice (⑥ single or combination.)	BM↓, Hepatotoxicity (Dose dependent S/E)	CBC, LFT - 3 monthly
	Back bone of Biologicals	MTx induced ILD unpredictable Permanent C/I to MTx use	CXR, PFT Baseline & Annually
		Teratogenicity	Counseling
HYDROXY-CHLOROQUINE	safest in ⑥ + 2nd choice	Bull's macula pathology (irreversible)	Fundus, Exam, Perimetry Baseline & annually SOS
SULFASALAZINE	Safe in ⑥ + 3rd choice	Gastritis Hepatotoxicity	LFT - Baseline + 3 monthly
LEFLUNAMIDE	Approved as Mono Rx Completed Family MODEST efficacy (limited use)	No synergy w other DMARDs 6x ↑ Hepatotoxicity Teratogenicity	Stop ≥ 2 ovulatory cycles before conception.

BIOLOGICALS = Pathophysiology of R.A.

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↑↑↑ Pro-inflammatory cytokines

TNF α most potent

(MOST PREFERRED)

Anti-TNF α agents

+ IL-1

ANAKINRA

IL-6

TOCILIZUMAB

Stimulates T cell

MODULATOR = ABATERCEPT

+

Stimulates B cell

RITUXIMAB

Intracellular signalling pathways of inflammation

e.g. ~~JAK~~ JAK - Janus associated Kinase

TOFACITINIB - Tyrosine kinase Θ of
JAK. - 1st oral Biological

ANTI - TNF α AGENTS		ADALIMUMAB, GOLIMUMAB
ETARNACEPT	INFliximab	S/C every 2-3 wks

~~ETARNACEPT~~

chimeric form
Mab against
TNF α receptor

Limited
efficacy

Common

INFliximab

chimeric Mab
against
TNF α itself

Excellent
efficacy
Anaphylaxis

PEGYLATED CERTOLIZUMAB

Fully Humanised MAb
against
TNF α itself

Equal efficacy
Safety

S/C every
6-8 weeks

Common ADR \Rightarrow Reactivation of TB.

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Hence, Screening for active dormant TB is mandatory before Anti-TNF α agents.

Tuberculin (MANTOUX)

\rightarrow MOST SENSITIVE.

\rightarrow BCG vaccination.
(false +ve)

WHO \rightarrow In countries (BCG vac.)

Best screening Test is

Interferon γ assay

(TB-GOLD/ quantification)
quantiferon

SPONDYLOARTHO PATHY

Group of Disorders characterised by

COMMON FEATURES

- 1) Seronegative RAF -ve
- 2) HLA B27 +ve Strong family History
- 3) 1° site - "Enthesis" Junc' Btw Bone & Tendon.
- 4) Axial Involvement is not Uncommon.
- 5) Extraarticular manifestations predominate
- 6) Excellent response to NSAIDs \rightarrow 1st Line of Rx

SpA are D/D - Inflammatory Polyarthritides

I

ANKYLOSING SPON. / BECHETROW'S / MARIE-STRUMPELL DISEASE³⁵

Epid - 10-20yrs, ♂ > ♀, 90% - HLA B27

C/F ARTICULAR
(Axial Dominant)

Sacro-iliac Joint - H/C	LBP (non-specific) always B/L But asymmetrical
Lumbar spine	Restricted esp. movement toward bending
Thoracic spine	Restricted Help. movement
Cervical spine	Highest risk of # in Lower part of Cx spine

EXTR-ARTICULAR
(Predominant)
70% → Recurrent U/L
ANT. UVEITIES

A

BEFORE

Spine Involvement

AFTER

HLA-B27 → +ve
-ve
~~X~~

≥ 2 common features
of SpA

(confirms A.S.)

MRI proven Sacroileitis

≥ 1 common feature of SpA

NORMAL	STAGES	Rx
vertebral Body	ENTHESIS	NSAIDS 136
Tendon of Paraspinal Muscle	MARROW EDEMA	BEST TIME for Biologicals.
	MARGINAL SYN DESMOPHYTES (unique feature)	DMARDs
	FUSION (ANKYLOSIS)	Biologicals (All TNF α agents)

MRI is mandatory

Only Test → Detect the stage of A.S.

Rx - UNFAVOURABLE

unlike RA only 10-15% active complete Remission

II PSORIATIC	III ENTEROPATHIC	IV REACTIVE
M/c - "Guttate" Pustular type of psoriasis	M/c - U.c. / Crohn's Disease <u>Common Pathology</u> Bowel Disease & Severity of activity Severity of arthritis	Post - infective F. / UTI CHLAMYDIA URBAN S. Typhi Travel Shigella Diarrhoea
M/c - ONCHOLYSIS' (nail pitting) Skin Lesions 10% urethritis ant ↓ Symmetrical polyarthritis (Predom - small jts) mimic RA - 5-10% pts arthritis > skin changes	M/c - Diarrhoea Most-specific = Pyoderma gangrenosum (Unique in U.c.) ↓ Asymmetrical polyarthritis (Predom - Large jts)	M/c → febrile illness → KERATODERMA BLENNORRHAGIA (Keratotic, Painless plaques - sole + Palm) ↓ Asymmetrical - polyarthritis (Predom - wt bearing jts)

- Early DIP jt \oplus
 X-Ray \rightarrow pencil in cup deformity
- MTx
 - Anti-TNF α agents
 - Tofacitinib.

Sulfasalazine
 Anti-TNF α

CHICKENGUNYA ARTHRITIS

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Hydroxychloroquine
 (additional anti-inflammatory action)

CRYSTAL INDUCED

GOUT		PSEUDO GOUT	
Crystal	Mon. Sodium urate (M.S.U.)	Ca^{2+} pyrophos. dihydrate (C.P.P.D)	
Epid	30-50 yrs $\sigma > \varphi$	> 50 yrs $\sigma > \varphi$	
Etiopath	90% - Renal Defect in Urate excretion. 10% - Diet / Drugs (Pyrazinamide / Thiazide)	90% - Jt. Degeneration. 10% - Hypercalcemia = Severe PTH adenoma So, early Paraneoplastic Syn	
C/F	Acute - Inflammatory MONO- ARTHRITIS (M/c - 1st MTP, ankle jt)	Acute, inflammatory OLIGO (M/c - Knee, Hips, shoulder)	
Screening	Serum Uric Acid	NON-SPECIFIC NORMAL VALUE DOESN'T exclude	S. Ca^{2+}
Synovial Fluid Analysis	NEEDLE SHAPED	RHOMBOID SHAPED	
Polarising microscopy ↓ Demonstrate crystals	STRONG +ve Birefringence Gold Std.	MILD +ve Refringence	

Rx

Acute Attack

Colchicine
Canakinumab

MAB
IL-1 β

NSAIDs

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Renal Failure

FEBUXOSTAT (X-O-I)

Hepatic excretion.

Additional anti-inflammatory

Intra-articular
steroids

Chronic
Prevention

TARGET Uric acid < 6mg/dL

1st Line = X-O-Inhibitors

(Allopurinol, Febuxostat)

Refractory cases

PEGLOTICASE

Regulated uricase
debulking action on
tubules

Encourage Physio
therapy

Avoid unnecessary
 Ca^{2+} /vit D₃
supplements

In elderly
Majority require
Jt. Replacement Sx.

Unfavourable

Prog

Favourable

CHARCOT'S

139

1st described → Tabes (Neurosyphilis)

Associations :- HI = DM, Leprosy, Amyloidosis

Pathophysiology

NEUROVASCULAR

Autonomic neuropathy



Disrupts Micro-circulation

NEURO-TRAUMA

Sensory neuropathy



Recurrent Microtrauma

DEGENERATION



Loss of pain sensation
(neuropathic jt)

M/C Forefoot Jt → Hind foot Jt → Ankle Jt

Ass XR → "Loose Bodies" in jt. cavity

Only Rx Strict Immobilization → Total Rest



facilitate recovery of
Jt.

only palliative → Unfavourable Prog.

VASCULITIS

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Ⓐ Based - Pathological Mechanisms

ANTIBODY (ANCA) MEDIATED	IMMUNE-complex MEDIATED	T-cell mediated
Wegener's (W.G.)	Hep. B - PAN	Giant cell arteritis
Churg Strauss (C.S.S.)	Hep C - Cryoglob	Takayasu's
M.P.A.	H.S.P.	W.G.
Microscopic polyangiitis	(Henoch-Schonlein Purpura)	C.S.S.

Ⓑ Based - Size of vessel affected (Preferred)

LARGE	MEDIUM	SMALL
Giant cell arteritis	Polyarteritis nodosa	
Takayasu	Kawasaki	
↓		
ANCA +ve		ANCA -ve
Anti-PR3	Anti- MPO	H.S.P. vs Hypersensitivity
W.G.	M.P.A.	Cryoglobulinemia
	C.S.S.	BECHET's Disease

G.C.A.

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>50 yrs, ♀ > ♂

C/F → Artery Involved (Carotid)

Ble. of EXTERNAL CAROTID	Ble. of INT. CAROTID	PATHOLOGY
H/c - <u>Sub. Temporal</u>	1st Br. Ophthalmic A.	Polymyalgia Rheumatica
Headache (worse-subpine)	End artery - No collaterals	
± Diplopia		
± Jaw claudication Pain	↓ Permanent BLINDNESS	
± Paresthesia over Jaw		

ESR (screening) >60 (significant)

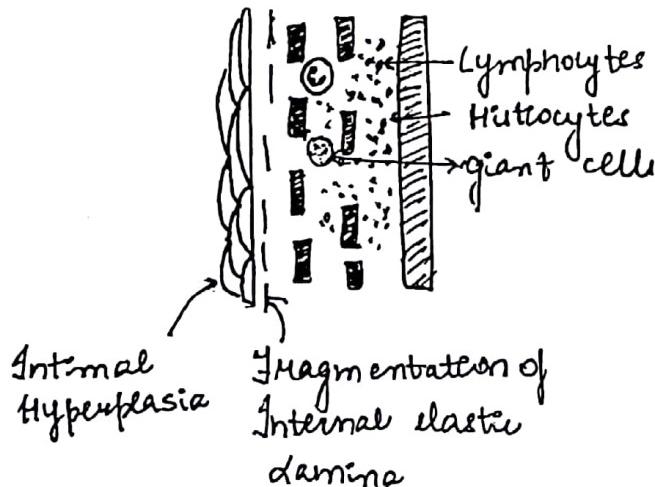
Gold Std →

- ↳ Temporal A. → Minimum > 2 cm Length.
- ↳ Biopsy → HPE - Granulomatous vasculitis

Rx = Steroids → Relief of symptoms

↳ only drug ⊂ prevent dreaded complication
= BLINDNESS

Early Rx = GOOD ↗ PROGNOSIS



TAKAYASUS / AORTIC ARCH SYNDROME

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Epid - 10-20 yrs, $\text{♀} > \text{♂}$

C/F - Depends on artery involved = All direct Br. of AORTA

SUBCLAVIAN (H/c)	CAROTID VERTEBRAL	COELIAC	RENAL	CORONARY $< 1\%$
VIL claudication Unequal/ABSENT PULSELESS DISEASE	Recurrent TIA/Stroke	Chv. mesenteric Insufficiency	Refractory HTN (RAS)	Acute Coronary Syndrome

Δ - CT - AORTOGRAPHY Gold Std

Rx - Immunosuppression + Angioplasty
(specific) (Palliation)

POOR PROGNOSIS

KAWASAKI's / Mucocutaneous L.N. Syndrome

H/c vasculitis ; < 5 yrs, $\text{♂} > \text{♀}$

Replaced R.H.D. → H/c cause of cardiac death in children due to Acquired heart Disease

AHA Guidelines

H/c manifestation → Febrile episode

Any Fever - on/after 4th Day (min. dur 5 days)⁸⁰

If - 4/5 of following features are \oplus

1> 90% B/L non-exudative conjunctivitis

2> Erythema over extremities

3> Peri-anal Rash

4> Strawberry Tongue

5> non-suppurative single, cervical L.N.

Rx- IV Ig + Long term Aspirin prophylaxis

- Relieve symptoms
 - Reduces risk of coronary involvement to 4-6%
 - Cannot reverse coronary atherosclerosis

Dreaded complication : CORONARY ANEURYSM

RUPTURE (4-6% case)

THROMBOSIS 95% of cases

↓
Elective angioplasty prevents.

Prognosis - FAVOURABLE

ULINASTATIN :- Neutrophil elastase Inhibitor.
(New, approved) only IgG refractory case.

PAN	SYSTEMIC NECROTISING VASCULITIS	MPA (Part of PAN prior to) 1999
Epid.	30-50 yrs.	$0^{\circ} > \varnothing$

Etiology Classical H/C - Idiopathic

30% Chx. Hep B infection

<p>Pathology</p> <p>Immune complex Mediated</p> <p>↓ fibrinoid necrosis</p> <p>Bifurcation of Medium vessel</p> <p>↓ Microaneurysm formation</p>	<p>ANCA - mediated vasculitis</p> <p>↓</p> <p>Small vessel predominant</p> <p>↓</p> <p>70% Anti-MPO +ve.</p>
<p>c/F <u>H/C</u> 90% arthralgia</p> <p>HEMATURIA - <u>c out GN</u> (rupture of micro aneurysm)</p>	<p>-</p> <p><u>always due to GN</u></p>
<p>CNS -</p>	<p>Mononeuritis - multiplex (Neuropathy) - asymmetrical</p>

SKIN =

Raynaud's phenomenon

Digital gangrene, LIVEDO

Purpuric Rash

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Gonadal arteries
mimic torsion

Pulmonary
Spaeed
But bronchies
may be involved

Alveolar H^oge
(ANCA +ve → D/D - Good Pastuer's
Syndrome)

Asis - Exception

Biopsy - Gold Std

Renal angio-
new aneurysm @
Bifurcation of vessels.

Rx Immunosuppressants → Favourable Prognosis

WEGENER'S GRANULOMATOSIS.

or chronic Granulomatous angitis

30-50 yrs, ♂ > ♀

Closest D/D → Good Pastuer's.

C/F	Pulmonary	Renal	Eyes
H/c	<ul style="list-style-type: none"> Lungs • B/L abscess • Multiple thin walled cavity • Alveolar H^oge 	<ul style="list-style-type: none"> URT - u specific <u>H/c - ch4. sinusitis</u> • Nasal bridge deformity • Serous otitis media • Subglottic stenosis (change in timbre of voice) 	<p>↓ RPGN</p> <p>H/c - Pan-uveitis</p> <p>SKIN</p> <p>Purpuric Rash over L.L.</p>

Serology 70% Anti PR3 +ve (Wegener's Antigen)
(SCREENING) 30% Anti MPO +ve 945

Anti: Absence cannot exclude W.G.

BEST TEST → LUNG BIOPSY

Rx cyclophosphamide → favourable response
GOOD & PROGNOSIS

CHURG

CHURG STRAUSS (eosinophilia & granulomatous angitis)

30-50yo. ♂>♀

c/f

PULMONARY	RENAL	SKIN involvement
LUNG URTI		
Late onset asthma allergic rhinitis	RPGN	Purpuric/ urticular rash

W.G. can be differentiated by ocular involvement

Asy- short course of steroids

Lung Biopsy / skin Rx = eosinophilic
vasculitis

Rx - short course of steroids

favourable prognosis, long term remission

GOOD & PROGNOSIS

H.S.P. (ANAPHYLACTOID PURPURA)

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> 90% cases - occur < 10 yrs, age $M > F$.

ADULT H.S.P.

HYPERSensitivity
VASCULITIS

EPID - 20-40 yrs, $M > F$

Etiopath Post Infective H/C - preceded by URTI

PALPABLE PURPURA		
C/F	Distribution	Generalised
LL + Buttocks Common Abd. pain, Malena	Mucous memb. involvement	Uncommon
3-5% - IgA deposits on GBM - Gross Hematuria	Renal involvement	NEVER occurs
Capillaries	Site - Biopsy (Gold std)	Post capillary venule

Rx - Reassurance/ Self Limiting Disease.

ESSENTIAL MIXED CRYOGLOBULINEMIA (EMC)

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↓
usually indicate
Idiopathic cause

Majority = 90% = (2°) cause

✓ Multiple myeloma

✓ Chro. Hep. C., Hep B

Lymphoproliferative states

Pathophys:- Exposure to cold → cryoglobulins ppt
($T < 37^\circ\text{C}$) | ($\text{Ig} \subseteq \text{ppt.}$)

H/c - Skin capillaries

98% - multiple areas of skin

necrosis

Renal tubules

A.T.N. (direct toxicity)

Δsu - Incubate plasma in cold bath → ppt. \oplus

Rx + Prog - underlying cause (unfavourable)

BEHICET'S DISEASE → HLA B5 $\frac{1}{148}$

lepid - 30-50 yrs, ♀ > ♂ (worse in ♂)

MAJOR

Recurrent, painful,
oral aphthous
ulcers

MINOR

- 1) Recurrent superficial thrombophlebitis
- 2) Bl. Hypopyon
- 3) Erythema nodosum
- 4) Painful genital ulcers
- 5) Pathergy Test +ve

Skin Prick $> 5\text{mm}$ deep

↓
Induration $(+)$

Δsu - MAJOR + 2 MINOR - confirm.

Rx - Steroids - excellent response

Favourable Prognosis

FIBROMYALGIA (Pain Sensitivity Syndrome)

Epid - 30-50 yrs, ♀ > ♂

Risk - Stress

Pathophys - ↓ Blood flow to Thalamus

(MINOR) ↓ cortisol response to stress

C/F - Multiple aches + pains (somatic complaint)
≥ 3 months

- Associated w Defect of NREM sleep

Ass - Clinical - 18 point pain testing (screening)
(> 11/18 +ve tenderness → significant)

MR spectroscopy - gold std.

Rx - Pregabalin.
Gabapentin
TCA
SSRI.

Unfavourable Prognosis → Prone to analgesic abuse
Poor Q.L.I.

CHRONIC FATIGUE SYNDROME

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20-40yrs, ♂ > ♀

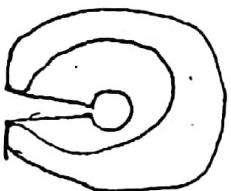
e/F - FATIGUE ≥ 6 weeks

Ass - of exclusion

- 1) Obesity
- 2) Substance abuse
- 3) All medical causes

- 1) Nutritional
- 2) Endocrine
Hypo thy, DM.
- 3) Ch4- Infection
- 4) autoimmune
- 5) neoplasm

Rx = Lifestyle Modification



RESPIRATORY

LUNG DEVELOPMENT

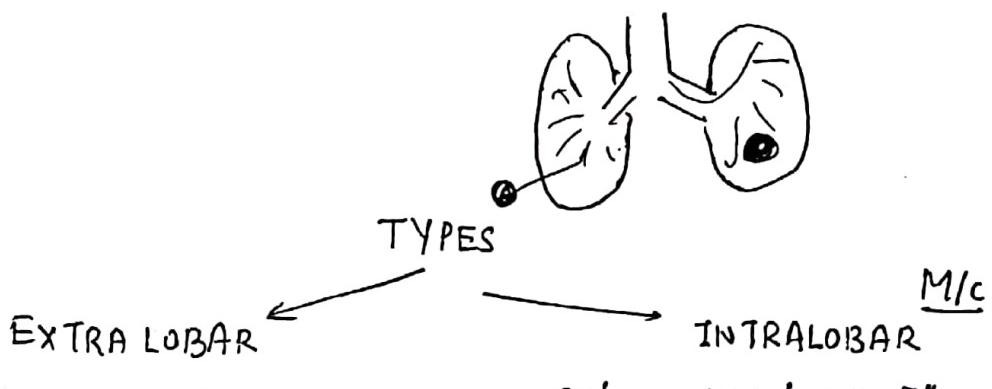
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5 stages

- 1) Embryonic stage → Lung buds
- 2) Pseudoglandular Stage → upto terminal Bronchiole
- 3) Canalicular - Alveolar ducts
- 4) Saccular - Primitive alveoli
- 5) Alveolar - Mature alveoli

BRONCHOPULMONARY SEQUESTRATION

Defn: Separation of part of lung during development from tracheobronchial tree & separate blood supply.



Separated & having
separate covering

M/c
separated part in adjacent lung
of ~~or~~ & covered by lung's pleura

M/c site → (L) lower lobe post basal segment

M/c Blood → Thoracic aorta
supply

IOC:- CT Angiography or MR angiography

Rx- Resection if pt. is symptomatic

SURFACTANT

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- 1) Dipalmitoyl Phosphatidyl choline / Lecithin.
- 2) Produced by Type II pneumocyte
- 3) also by Clara cells.
- 4) Removed by Alveolar macrophage

5) Functions :-

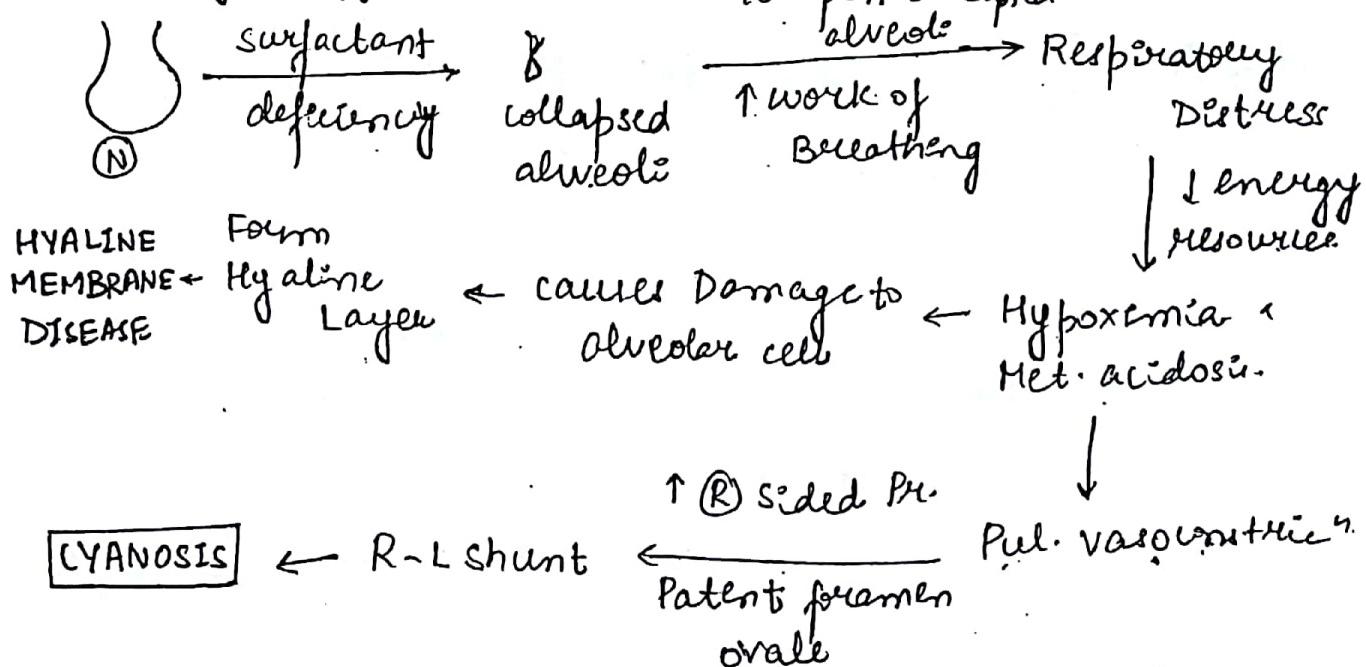
- a) surface Tension ↓
- b) maintain alveolar stability/ FRC
- c) Compliance

6) Surfactant "index" starts at **20wks**

Peak at **35wks**

So, if < 35wks → Respiratory distress syndrome
or
Hyaline membrane Disease.

Pathophysiology of RDS



X-Ray Findings :-

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- 1) Reticulo granular granular pattern
- 2) Ground glassing
- 3) white out Lungs
- 4) ↓ lung volume
(↓ FRC)

Inv :-

Lecithin > 2 ⇒ MATURE LUNG.

Sphingomyelin

Rx :- mild to moderate ⇒ O₂ + CPAP

Severe ⇒ Invasive Mech. ventilation +
Surfactant Deficiency Replacement

Surfactant [Hyaline appear pink on Biopsy]

PULMONARY ALVEOLAR PROTEINOSIS

Surfactant clearance is impaired

Etiology :- 1° form (M/C) → Auto Ab against GM-CSF

2° form → ✓ Acute Silicosis
✓ Haemato poetic malignancy
✓ Immunodeficiency

Silica particles are toxic to alveolar macrophage
Ch. Silicosis pt. are prone to TB.

In malignancy, macrophages are not matured enough
to carry out func.

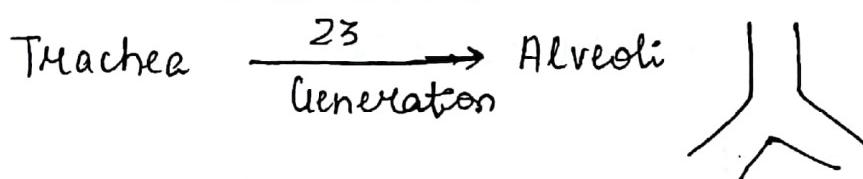
In immunodeficiency, macrophages ↓

Pathophysiology -
 ↓ Diffusion from O_2 → Hypoxemia. 155

- Δ :- alveolar
- 1) Broncho pulmonary Lavage → milky white
 - 2) BAL → PAS +ve
 - 3) CT Chest → CRAZY PAVING PATTERN

Rx - Whole Lung Lavage

WIEBELS LUNG MODEL

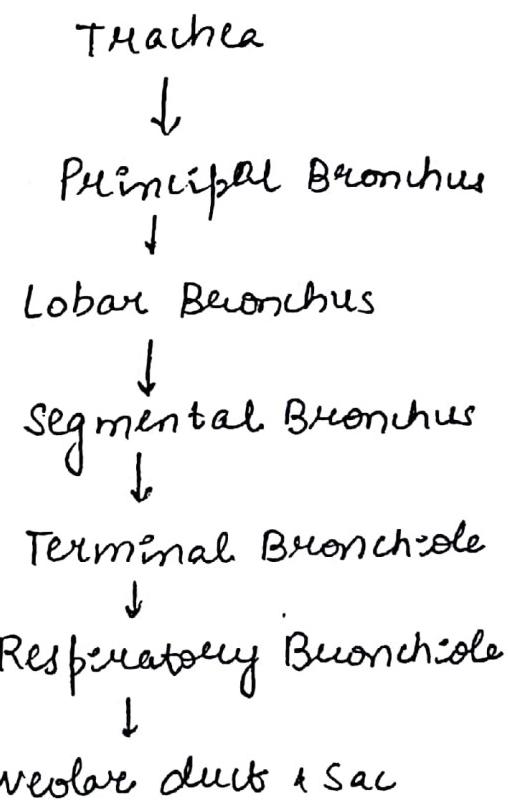


Functional / ventilatory unit/
 Acinus = Distal to terminal Bronchiole

Radiological unit / 2° Pulmonary Lobule

= Roof of a group of acinus (5-7)

involved in EMPHYSEMA



upto terminal Bronchiole = Conducting Pathway

(R) Main Bronchus

Aspiration is more common
 this side as it is short,
 stout, straight

(L) Main Bronchus

Bronchiectasis more common
 in (L) lower part → narrow
 angulated & drainage

BPS Segments + ASPIRATION PNEUMONIA

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M/c segment involved in Asp. Pneumonia =

⑧ Lower Lobe superior

/ seg or ⑧ upper

M/c segment involved in Asp. Pneumonia in supine Lobe Post

Lobe

Post

" " " Asp. Pneumonia in sitting /standing
= ⑧ Lower Lobe posterior Basal

" " " Asp. Pneumonia in Bending forward
⑧ middle Lobe

Best Inv:- **Bronchoscopy**

HEMOPTYSIS

Lung → High Pr. Systemic circulation ⇒ Bronchial artery
↓ Low Pr. Pulmonary " ⇒ Pulmonary artery

M/c source of hemoptysis → Bronchial artery

M/c source of massive hemoptysis ↑

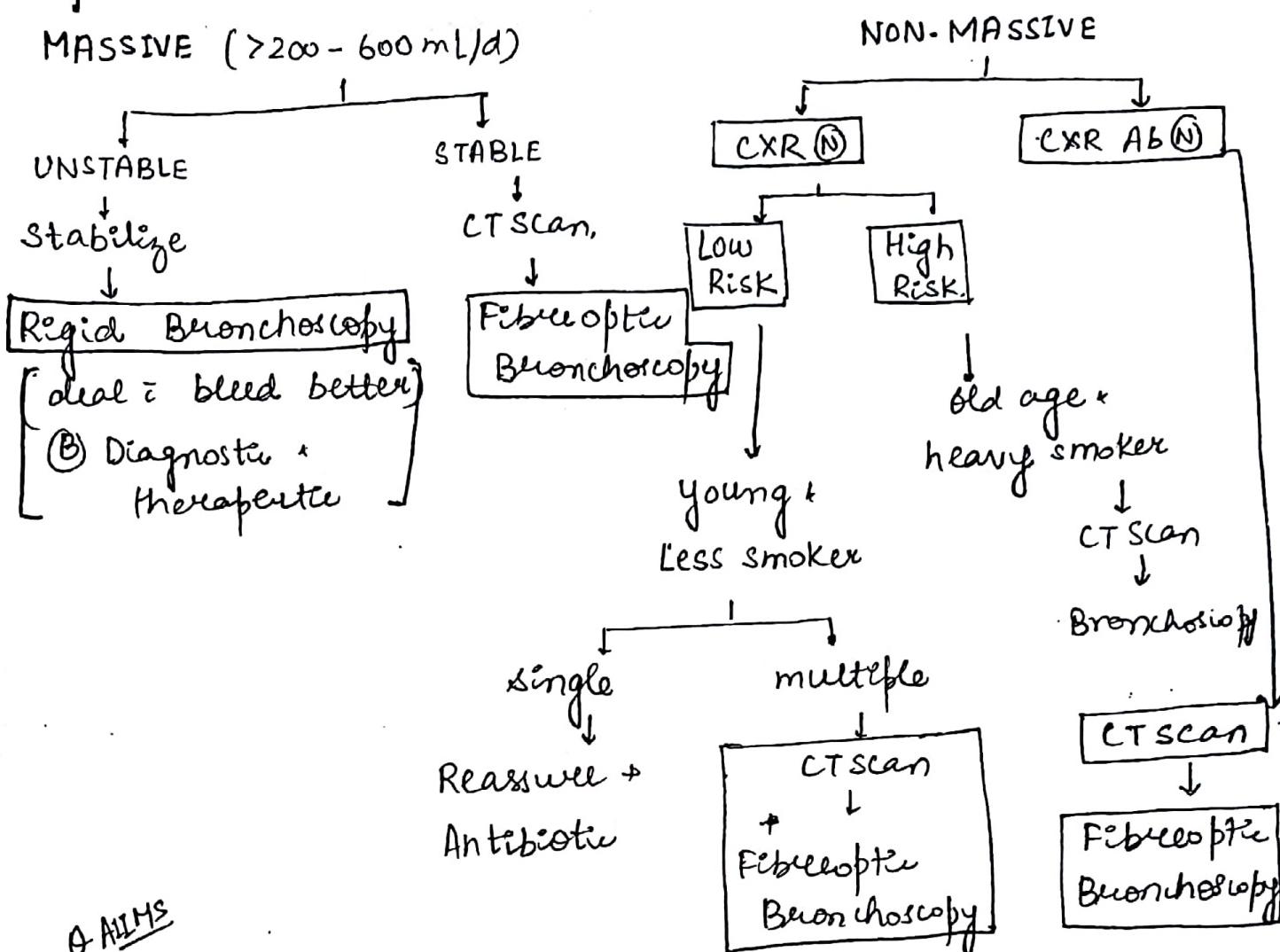
M/c of hemoptysis in India → TB

M/c of " worldwide → TB

M/c of Death in hemoptysis → Asphyxiation. ↓ Blood clot.

APPROACH TO HEMOPTYSIS

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AIMS

PERSISTENT CASES-

Br. artery embolisation

Resection of affected lobe

Source of hemoptysis in Mitral Stenosis =

[Rupture of Pulmonary Bronchial
venous connec. → Br. veins]

Source of hemoptysis in Pulmonary Embolism → Pulmonary artery

H/C source of hemoptysis in TB → Br. artery

Rasmussen's aneurysm → Pulmonary artery

Rasmussen's

organism that causes pseudohemophy's
= *Serratia marcescens*

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INTRAPLEURAL PR.

Lung always tries to collapse to centre



Chest wall always tries to move outward

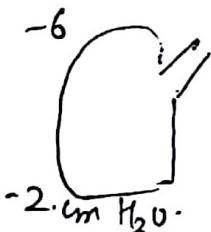


There is a Balancing force Between the 2

↓
-ve Intrapleural Pressure (IPP)

[Usually -ve during (N) respiration
Maintains equilibrium Lung volume \Rightarrow FRC / Relaxing volume]

(N) Value = -2 to -6 cm H₂O.



More -ve IPP

Deep Inspiration.

Pneumony

Collapse

Fibrosis

Less -ve IPP / +ve IPP

1) Forced Expiration.

* Cough, valsalva manoeuvre

2) Pushing lesions

3) * Tension Pneumothorax

* Maligne ..

COMPLIANCE

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- Stretchability of Lung.
- Change in unit volume per unit change in pressure

$$C = \frac{\Delta V}{\Delta P}$$

Static compliance = air flow & resistance not considered

Dynamic \rightarrow air flow + air resistance considered

EMPHYSEMA PATHOPHYSIOLOGY

Insp: Exp. = 2s : 3s early closure

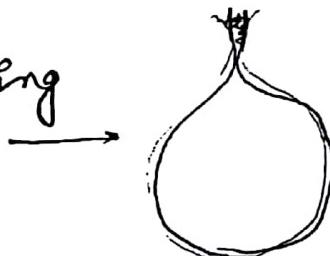


if elastic fibres

Damaged.



→ Air Trapping
emphysema at
end expiration.



Dynamic Hyperinflation

CXR

1) Bl ~~H~~ Hypertranslucency

2) Flat Diaphragm

3) Tubular Heart

4) Barrel shaped chest wall

↓ diameter of airway

↑ Airway resistance

↓ Dynamic compliance
in emphysema

Loss of elastic fibres
↑ static compliance

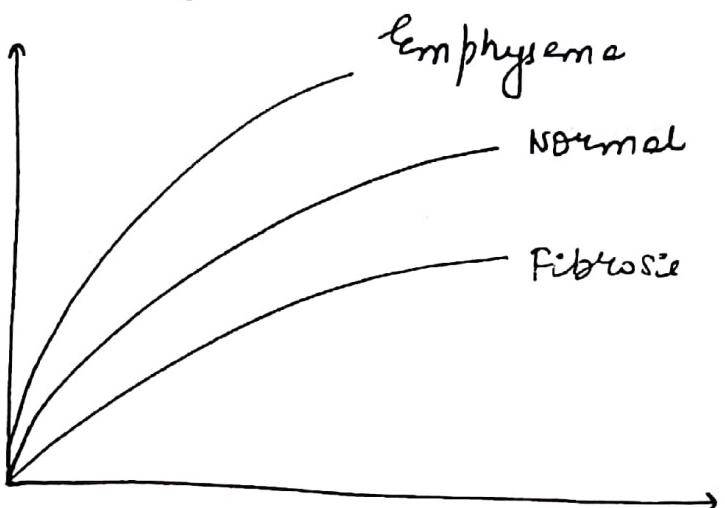
Emphysema -
RV ↑

FRC ↑

TLCT

- ↓ compliance
- 1) Surfactant Deficiency
 - 2) ARDS
 - 3) Pulmonary edema
 - 4) Fibrosis / ILD
 - 5) 100% O₂ damage

- ↑ compliance 160
- 1) old age
 - 2) Emphysema
 - Static compl ↑
 - Dynamic compl + (↑ airway resistance)



HOOVER's SIGN → Paradoxical inward movement of lower ribcage during inspiration
severe COPD

↓
since diaphragm is not there, that's why.

HISTOLOGY OF ALVEOLI

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TYPE I

Pavement epithelium
Vulnerable to damage
More surface area



TYPE II

Secretes surfactant
can divide & reconstitute
Type I cells
More No.

ZONES OF LUNG

Vertical regions based on hydrostatic Pressure

P_A = alveolar pressure

P_a = arterial "

P_v = venous "

Zone 1 = $P_A > P_a > P_v$

$P_A > P_a > P_v$

$P_a > P_A > P_v$

2 = $P_a > P_A > P_v$

$P_a > P_v > P_A$

3 = $P_a > P_v > P_A$

(N) Lung = combination of Zone II & III.

DEAD SPACE =

Area ventilated but no sufficient gas exchange (blood flow)

Anatomical D.S.

Physiologic D.S.

Ext. nares upto Terminal
Bronchiale.

PDS = Anat DS + Alveolar D.S.

Measured by Fowler's method

In (N) Alveolar D.S. = 0

N_2 used

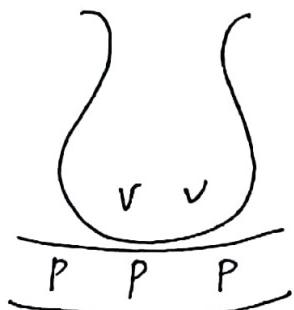
(N) P.D.S. = Anat D.S.

* Bohr's equation

\uparrow Anat D.S.

- 1> Neck extension
- 2> Bronchodilation
- 3> Old age

$\uparrow\uparrow$ Alv. D.s -



\downarrow Anat D.S.

- 1> Neck Flexion

2> Bronchoconstriction

3> Orotracheal intubation / Tracheostomy

Bypass
nasal airway

Bypass oral,
nasal airway

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COPD



wasted ventilation

=

P. Embolism



In P. embolism , predominant Defect is in Perfusion

MECHANISMS OF HYPOXEMIA

(I) V/P mismatch (H/lc)

(II) Shunt

(III) Diffusion Defect

(IV) Hypoventilation

II SHUNT-

Bypass of blood \rightarrow out oxygenation.
(Diversion)

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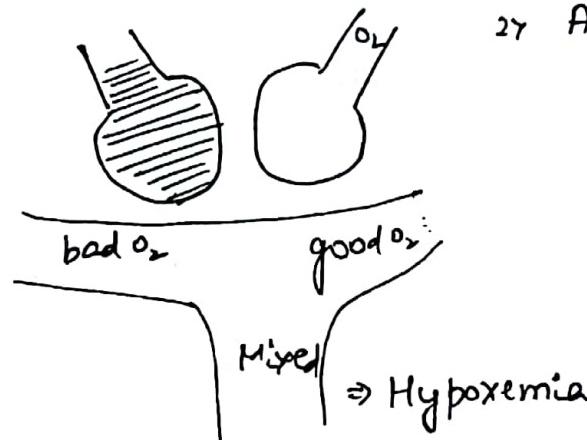
INTRACARDIAC

R → L shunt

INTRAPULMONARY

⇒ Sev. Pneumonia

⇒ ARDS



Less responsive to supplemental O_2 .

Rx = Mechanical Ventilation.

Rx infection.

Cure pathology.

$\frac{V}{P}$ Ratio

Max. Ventilation
Max. Perfusion
Min. V/P ratio

Min. ventilation.
Min. perfusion
Max. V/P ratio

	V	P	V/P	PAO_2	$PA CO_2$
APEX	2 L	0.5 L	4.	130	28
MIDZONE	4 L	5 L	0.8	104	35
BASE	6 L	10 L	0.6	92	42

1° TB \Rightarrow Mid & Lower Lobe

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2° TB \Rightarrow Apex.

↳ active disease due to proliferation of Bacilli

Reason

$\uparrow O_2$ tension

$\uparrow V/P$ ratio.

DIFFUSION CAPACITY OF LUNG \equiv $DLCO$

↓

↑ DLCO

1) Fibrosis o/ ILD

2) Severe emphysema

3) Pneumonia

4) ARDS

5) Sarcoidosis

6) P. embolism

7) Anaemia

8) Pul. HTN

No blood flow exchange

↳ Polycythaemia

2) Exercise (\uparrow Blood flow)

3) Alveolar H_ge

↳ good pastewi's
Wegener

4) Acute Asthma

↳ sed eosinophil inflammation

↓ NO produc"

P. vasodilatation

↑ DLCO

New FeNO = Test for Acute Asthma

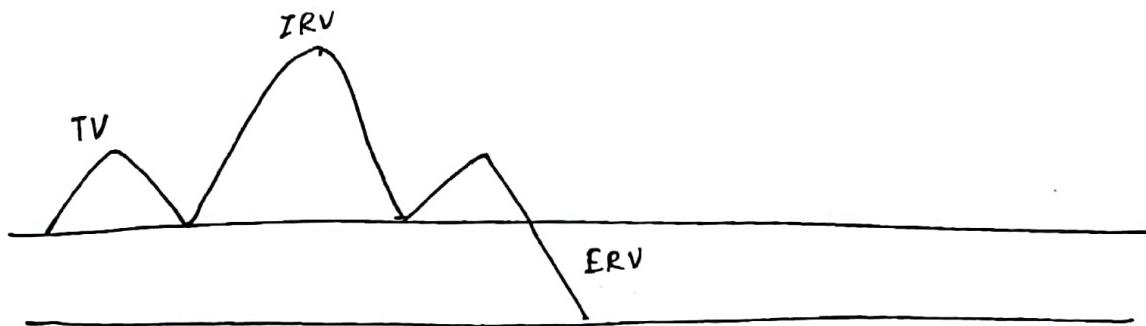
SPIROMETRY

Tidal volume = Normally in/out = 500 mL^{165}

IRV = air accommodated to effort after Tidal inhalation = 3000 mL

ERV = air expired to effort after Tidal expiration = 1100 mL

RV = Air that remains after ~~flex~~ forcible expiration = 1200 mL



VC = Volume exhaled forcibly after max. inhalation.

$$TV + ERV + IRV$$

$$IC = TV + IRV$$

$$FRC = ERV + RV$$

$$TLC = \underbrace{TV + IRV + ERV + RV}_{VC} + \underbrace{ERV}_{FRC} + IC$$

Conventional Spirometer = can't measure

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- RV
- FRC
- TLC

Methods for $\left. \begin{matrix} \text{RV} \\ \text{FRC} \\ \text{TLC} \end{matrix} \right\}$ He Dilution Method
N₂ washout

Body Plethysmography. (Best)

DYNAMIC LUNG VOL

1) Forced Vital Capacity = Rapid & forcible VC

$$\boxed{\text{FeV}_1} = \text{FVC} @ \text{end of 1st sec} = 80\%$$

2) Timed Vital Capacity → $\boxed{\text{FeV}_2}$ FVC @ end of 2nd sec = 90%.

$$\boxed{\text{FeV}_3} \quad \text{FVC} @ \text{end of 3rd sec} = 98\%$$

3) PEFR = Peak expiratory Flow Rate

→ Peak of FVC

→ Indicates large airflow flow

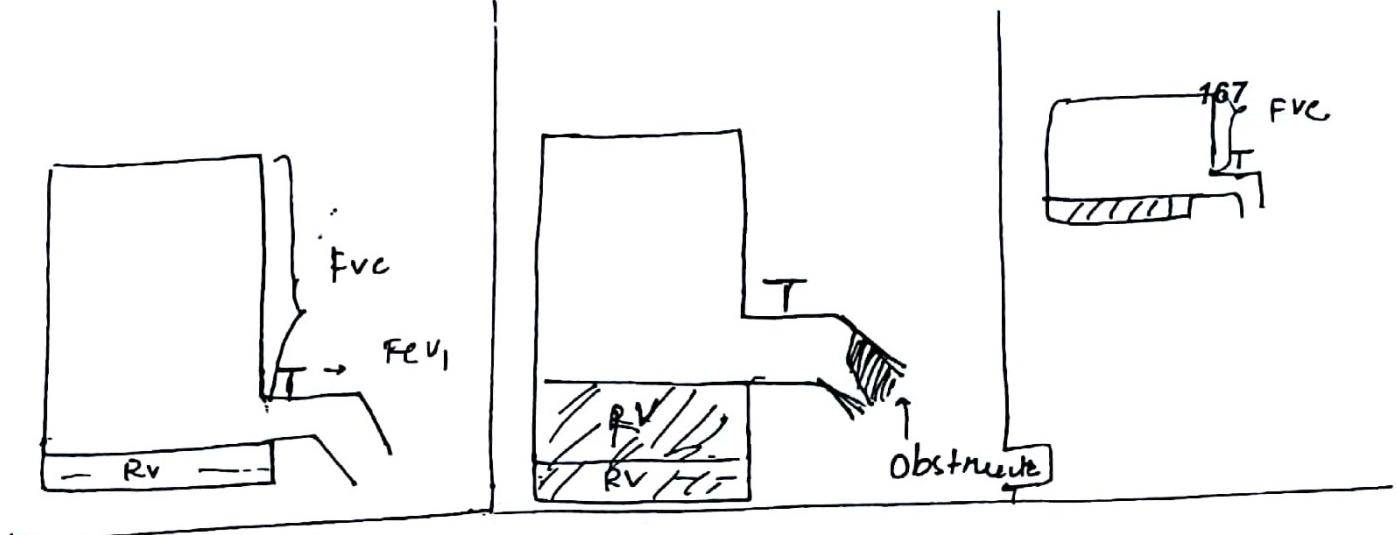
→ 400-500 mL/min

4) MEFV → Avg. velocity during mid portion of exhalation.

→ sensitive indication of small airway function

→ 300 mL/min

<u>N</u>	<u>OBSTRUCTIVE</u>	<u>RESTRICTIVE</u>
FVC <u>N</u>	FeV ₁ ↓↓	FeV ₁ <u>(N)</u> ↓
FeV ₁ <u>N</u>	FVC <u>N</u>	FVC ↓↓
$\frac{\text{FeV}_1}{\text{FVC}} = \underline{\text{N}}$	$\frac{\text{FeV}_1}{\text{FVC}} = \downarrow \downarrow$	$\frac{\text{FeV}_1}{\text{FVC}} = \uparrow / \underline{\text{N}}$



OBSTRUCTIVE

- 1) Asthma
- 2) Bronchiectasis
- 3) COPD
 - ChE. Bronchitis
 - Emphysema

RESTRICTIVE

- ↓ ↓
- Intrinsic RLD Extrinsic RLD
 - Pul. parenchyma Pul. parenchyma
involved unininvolved.

- | | |
|---|--|
| <ul style="list-style-type: none"> 1) Fibrosis 2) Pneumonia 3) Sarcoidosis 4) Occupational lung
disease | <ul style="list-style-type: none"> 1) Kyphoscoliosis 2) Neuromuscular
Disease <ul style="list-style-type: none"> a) GBS b) Poliomyelitis c) Myasthenia
Gravis d) Amy. Lat Sclerosis 3) Diaphragmatic
Dysfunction |
|---|--|

EMPHYSEMA

1) Obstructive

$$2) \frac{FeV_1}{FVC} \downarrow$$

3) RV↑, FRC↑, TLC↑

4) Compliance

Static $\frac{1}{C_{DLCO}}$ ↑
Dynamic $\frac{1}{C_{DLCO}}$ ↓

FIBROSIS / ILD

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1) Restrictive

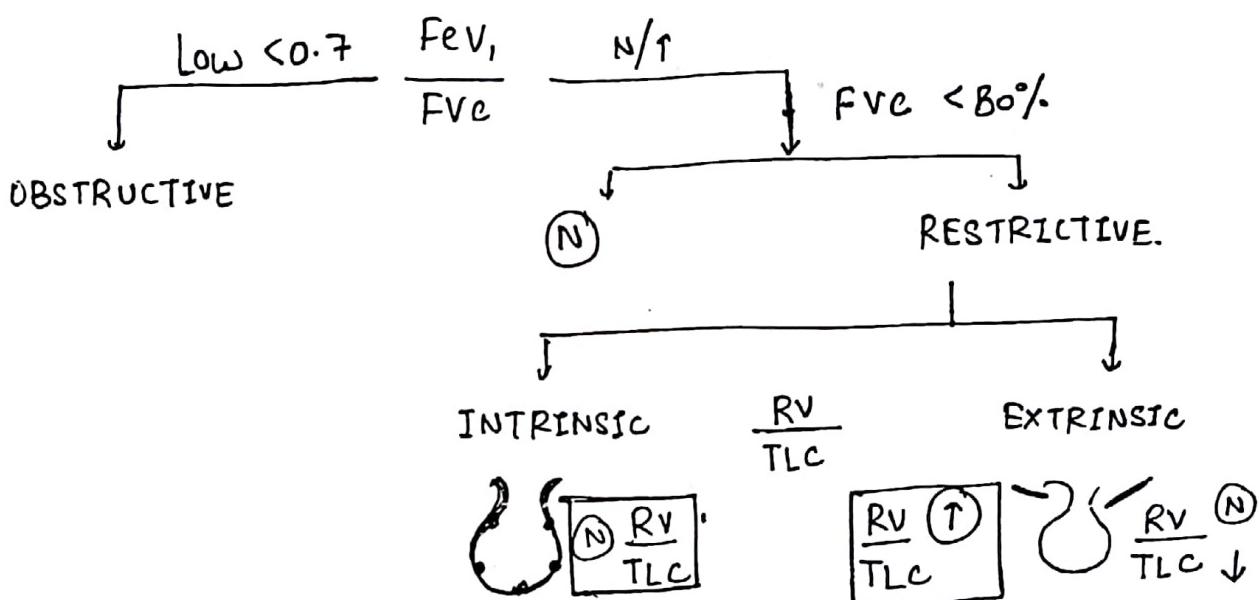
$$2) \frac{FeV_1}{FVC} \uparrow / \textcircled{N}$$

3) RV↓, FRC↓, TLC↓

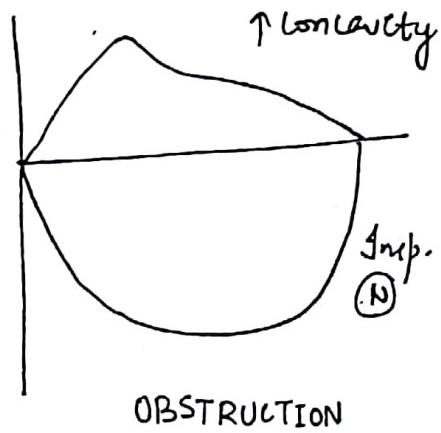
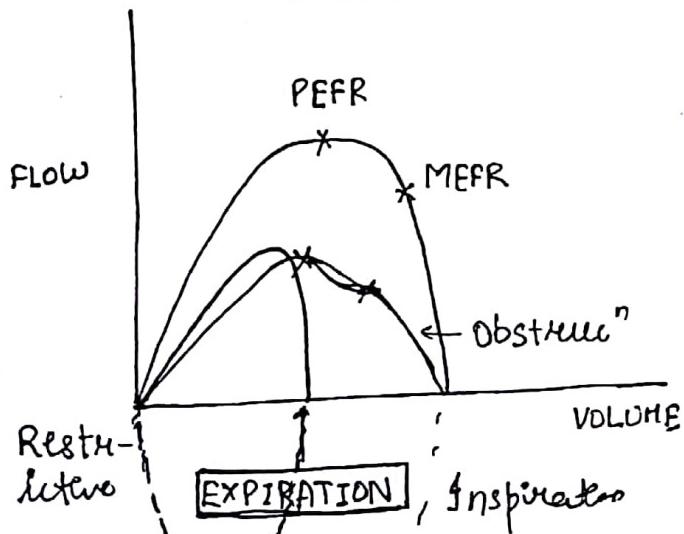
4) Compliance ↓

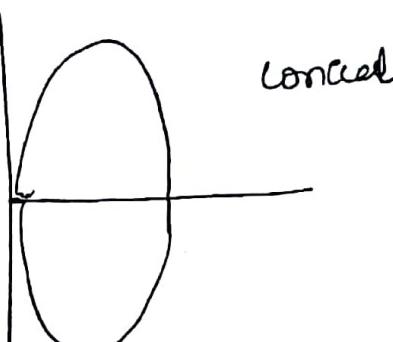
5) DLCO ↓

INTERPRETATION OF SPIROMETRY

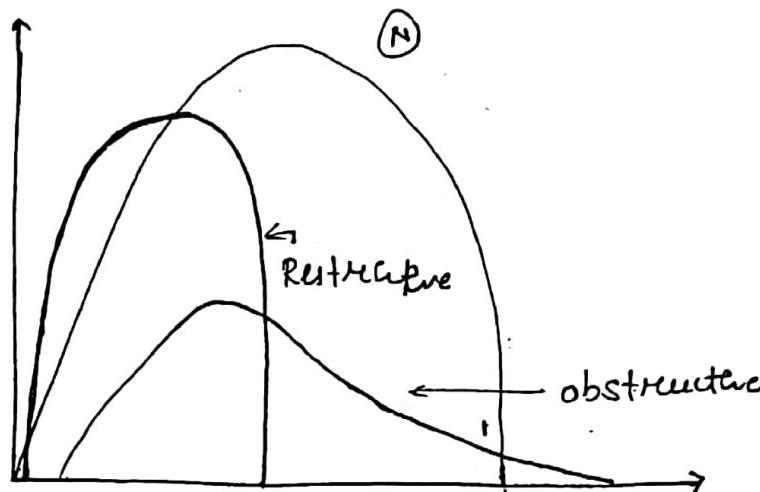


FLOW VOLUME LOOPS





RESTRICTIVE

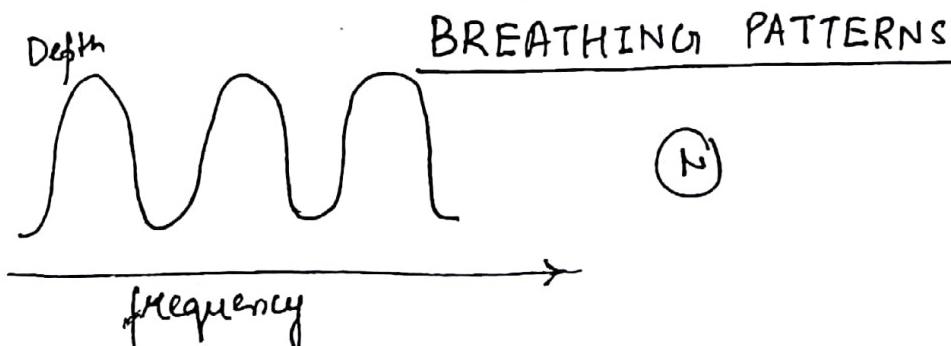


$$\text{If } \frac{\text{FeV}_1}{\text{Frc}} \text{ } \textcircled{N} \Rightarrow \text{All } \textcircled{N}$$

Isp_{O_2} on ~~less~~^{more} exertion

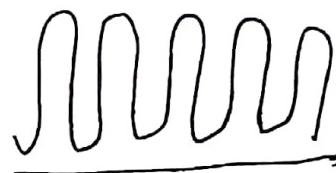
↓ DLCO ↓ (young ♀)

10 Pulmonary HTN



KUSSMAUL'S BREATHING :-

Rapid 'Deep' Breathing

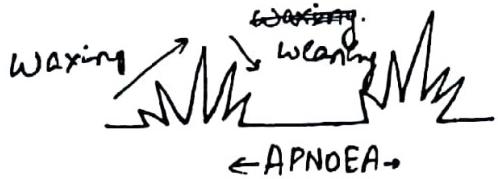


e.g. sev. Metabolic acidosis \rightarrow DKA, Uraemia

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2) CHEYNE STOKES BREATHING.

\rightarrow Periodic Breathing \equiv cyclical Pattern.



\rightarrow altered response to CO_2 .

e.g. CHF, narcotic overdose, Head injury

3) BIOTS BREATHING

\rightarrow Irregular respiration \equiv Apnoea

e.g. Meningitis
 \uparrow ICP



4) ATAXIC BREATHING

Inregularly irregular respiration \equiv \uparrow Apnoea



e.g. Brainstem injury.

BREATH SOUNDS

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Ab (N)

- (N) → vesicular Breathing
- Similar to sounds of Hustling of leaves
- Low pitch, soft
- I:E = 3:1
No pause.

- Bronchial Breathing
- Similar to tracheal sound
- High pitch, Harsh
- I:E = 1:1
pause

- 1) Tubular Breathing → Consolidation
- 2) Cavernous " → cavity
- 3) Amphoric " → Metallic quality
e.g. Bronchopleural fistula

ADVENTITIOUS BREATH SOUNDS :-

WHEEZE (musical)

Produced when airflow past an obstruction due to vibration of airways

Monophonic
Local involvement

e.g.
Bronchial Tumour

Rhonchi :- Low pitch wheeze

Polyphonic
Diffuse involvement

e.g.
Asthma, COPD

CREPTS/ CRACKLES/ RALES

Non-musical sounds

1) When air flows into secretions

⇒ Bubbling noise

cause crepts

BRONCHIECTASIS

2) When alveoli suddenly pop open during inspiration



ILD



Fine crepts

(B) Fine & Coarse Crepts

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- 1) P. edema (fine > coarse)
- 2) Pneumonia
- 3) TB

STRIDOR - Loud, audible, inspiratory & expiratory wheeze

due to Laryngospasm

F.B.

Laryngeal edema

Subglottic stenosis

LES-

PULLING	NO PULL/PUSH	PUSHING LESION
Collapse Fibrosis	Consolidation	Pleural effusion Pneumothorax
<u>Percussion</u> = Dull in collapse Impaired in fibrosis	Dull note	Stony dull in P. eff. Hyper-resonant/Tympanic in pneumothorax
Auscultation	Bronchial breathing +	BS ↓ to -
CXR	Atelectasis Bronchogram	Pl. eff = white meniscoid fluid level.
collapse - Homogenous white		Pneumothorax = Black Ⓛ
Fibrosis - Heterogeneously white		compressed lung margin

~~P~~ PLEURAL EFFUSION

HYDROPPNEUMOTHORAX 173

Straight line of dullness	(-)	(+)
Shifting dullness	(-)	(+)
Suspirior splash	(-)	(+)
Sound of coin.	(-)	(+)

RESPIRATORY FAILURE

Low $\text{P}_{\text{O}_2} < 60 \text{ mmHg}$, High $\text{P}_{\text{CO}_2} > 45 \text{ mmHg}$.

(HYPOXIA)

(HYPERCAPNIA)

Type I RF - Hypoxemic RF

Type II RF - Hypercapnic RF

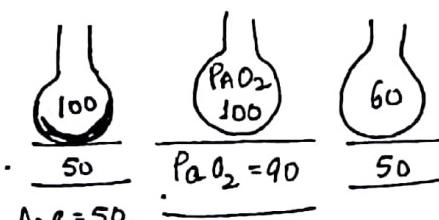
Type III RF - Perioperative RF due to lung atelectasis associated with general anaesthesia

Type IV RF - due to hypoperfusion of respiratory m/s due to shock.

TYPE I

Diffusion defect

↓ Transfer of O_2 .



$$\text{PAO}_2 = \text{N}$$

$$\text{PaO}_2 = \downarrow$$

$$\text{P}_{(\text{A}-\text{a})\text{O}_2} = \uparrow\uparrow$$

$$\text{Paco}_2 = \text{N}/\downarrow$$

TYPE II

Hypoventilation

↓ Resp. effort

$$\text{PAO}_2 = \downarrow$$

$$\text{PaO}_2 = \downarrow$$

$$\text{P}_{(\text{A}-\text{a})\text{O}_2} = \text{N}$$

$$\text{Paco}_2 = \uparrow$$

pH $\downarrow\downarrow$ (Respiratory Acidosis)

CAUSES

Pneumonia

ARDS

ILD

Pulmonary edema

P. Thromboembolism [Highest]
 P_{A-aO_2}

$R_x O_2 + R_x$ of underlying disease

If pt. not improving

Pneumonia

ARDS

Invasive +ve pressure ventilation preferred

CENTRAL CAUSE

Narcotic use

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Head injury

OBSTRUCTION

F-B.

Severe COPD

PERIPHERAL

Neuromuscular Disorder

DIAPHRAGM CAUSE

Palsy

\Rightarrow [COPD] - pneumothorax

$O_2 + R_x$ underlying cause

If pt. not improving

[COPD / NMD]

Non-invasive +ve pressure ventilation is 1st choice

NIPPV [BiPAP (NIV commonly used)
CPAP

If no response \Rightarrow IPPV

C/I of non-Invasive ventilation

- 1) altered sensorium
- 2) ↑ chances of aspiration
- 3) cardiac arrest
- 4) Hemodynamically unstable
- 5) Unco-operative pts.

- 6) Claustrophobic
- 7) Active GI Bleed 175
- 8) Recent Facial Trauma or Sx.

ARDS

Defn:- Acute shortness of Breath + Hypoxemia + Diffuse Pulmonary infiltrate

Causes:-

DIRECT

- 1) Pneumonia
- 2) Aspiration of gastric content
- 3) Lung contusion
- 4) Near drowning
- 5) Toxin inhalation

INDIRECT

- 1) Sepsis (M/c).
- 2) Severe trauma
- 3) Blood: multiple Blood Transfusion.
- 4) Severe Burns.
- 5) Pancreatitis

OTHER NAMES :-

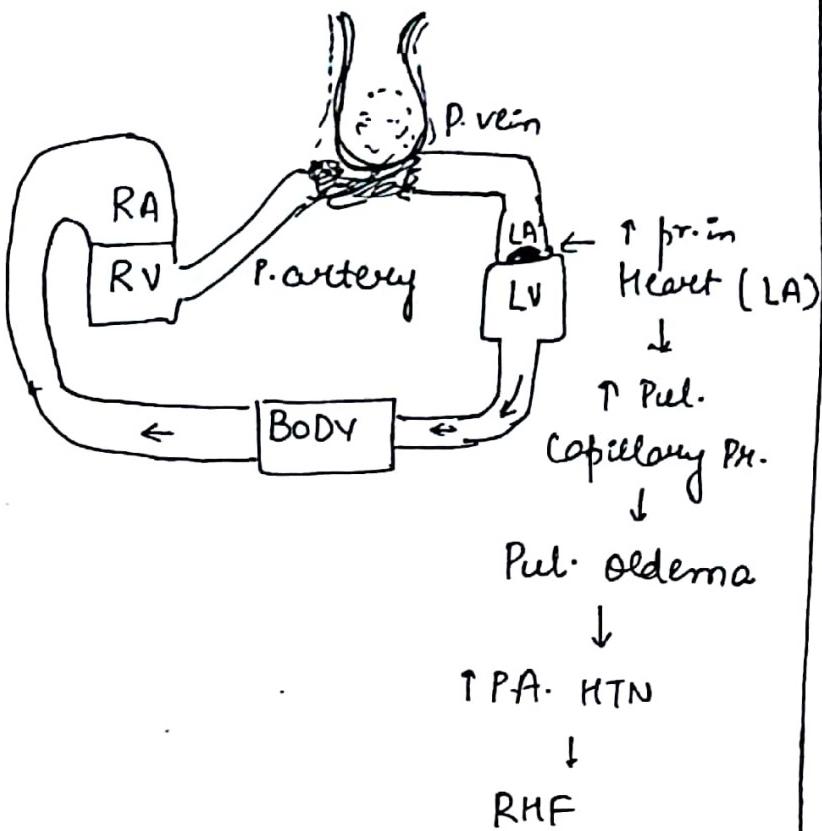
- 1> Noncardiogenic Pul. edema
- 2> ↑ permeability Pul. "
- 3> Low pressure Pul. "
- 4> Diffuse Alveolar Damage (most characteristic)
- 5> Shock Lung
- 6> Wet Lung

Pathogenesis

Cardiogenic P. edema

Non-cardiogen P. Edema

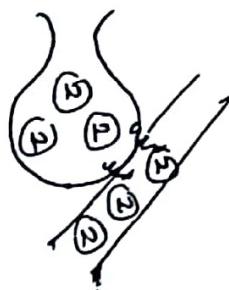
CARDIOGENIC P. Edema



PCWP = ↑ in CPE.

NON-CARDIOGENIC

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Damage to capillary endothelium + alveolar epithelium.

↑ Neutrophil entry
= inflammation.

↑ damage = ↑ inflammatory exudate.

SHOCK LUNG.

PCWP / Pul. Arterial Occlusion Pressure

→ Swan Ganz Catheter used

→ Indirect measure of LAP

→ In CPE PCWP > 18 mmHg

In NCPE PCWP < 18 mmHg

Assess Berlin 2012 Definition

1) Acute Onset < 7 days

2) Origin of edema → non-cardiogenic
PCWP < 18 mmHg

3) B/L diffuse infiltrate in CXR - PA

4) $\frac{PaO_2}{FiO_2} < \frac{60 \text{ mmHg}}{0.2} = < 300$.

$\frac{PaO_2}{FiO_2}$ 200 - 300 = Mild ARDS

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$\frac{PaO_2}{FiO_2}$ 100 - 200 = Mod. ARDS

$\frac{PaO_2}{FiO_2}$ < 100 = Severe ARDS

Rx

Most Recommended Strategy / Beneficial :-

1) Low Tidal Volume Mechanical Ventilation (4-6 mL/kg Body wt.)

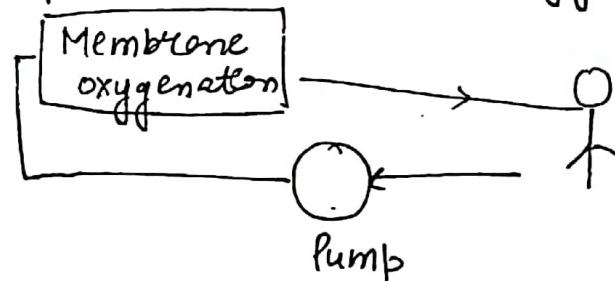
- Assist control mode to avoid ventilation associated Lung Injury

2) Adequate +ve end expiratory Pressure

3) Gluco-corticoid may be helpful.

* Newer Ventilation Mode :-

1) Extracorporeal Membrane Oxygenation.



Mech :- Blood is pumped into membrane oxygenator & oxygenates blood & sent back into body.

Beneficial in severe ARDS.

2) Prone Ventilation.

MECH.:- In prone ventilation, diaphragmatic pressure on lower alveoli ↓ ⇒ ↑ sed alveoli for oxygenation ¹⁷⁸
~~as wt. of abdomen ↑~~

For Benefit ⇒ Done for 16 consecutive hours.

- Helpful in improving oxygenation in pts w/ severe hypoxemia.
- Not helpful in pt. w/ pre-existing chest wall deformity / severe fibrosis.

3) High Frequency Oscillator Ventilation

- Low tidal volume are given w/ ~~more~~ ^{more} frequency
- Beneficial in few studies

TRALI

(Transfusion Related Acute Lung Injury)

- occurs in or during 6hr of transfusion.
- Donor Plasma antibodies vs Recipient leukocyte
→ Mediator release
- Feature of ARDS

Rx = supportive

H/ce of Transfusion related fatalities.

P. THROMBOEMBOLISM (M/e of cor. Pulmonale)

Migration of thrombus \rightarrow into Pulmonary artery¹⁷⁹
M/e source: Pelvic veins.

CAUSES

1°

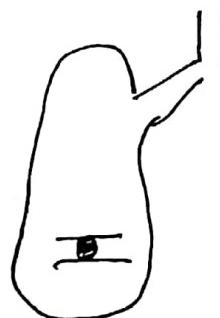
- 1) Protein c, s deficiency
- 2) Factor V Leiden mutation.
- 3) Lupus anticoagulant
- 4) Antiphospholipid antibody syndrome
- 5) Hyper homocystinuria

2°

- 1) Prolonged immobilization
- 2) Recent Trauma. Sx
- 3) High oestrogen state
e.g. ♀,
oestrogen containing pills
- 4) malignancy
- 5) Nephrotic syndrome

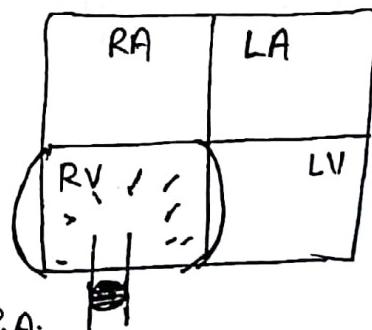
PATHOPHYSIOLOGY

LUNG



- 1) ↑ Pul. arterial Pressure
 \hookrightarrow rupture of vessel
Hemoptysis
- 2) ↑ Alv. Dead space = Hypoxemia
 \downarrow
Shortness of Breath.
- 3) ↑ Serotonin by platelets
 \hookrightarrow Bronchospasm \rightarrow airway \uparrow resistance

HEART



P.A.

↑ R.V. Pressure

RV Dilatation

RV Hypokinesia

Movement of septum into
LV \Rightarrow Ventricular

Interdependence

\downarrow
SHOCK [COR
Pulmonale]

4) Lung ischaemia → ↑ infl.
mediators

180

5) Pleuritis → chest pain

6) Pleural effusion → Exudate >>
Transudate

TRIAD

- 1) ⚡ Chest pain
- 2) SOB (M/c symptom)
- 3) Hemoptysis.

COR PULMONALE :- alteration in str. + function of
R ventricle due to 1° disorder of Resp.
System excluding disease of L heart

M/c of char. cor pulmonale → COPD

M/c of Acute " → Massive PTE

↓
presenting c shock

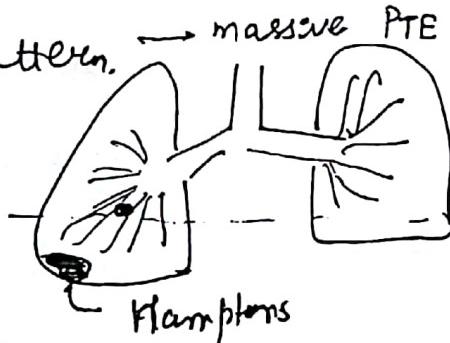
DIAGNOSIS

1) ABG → Type I Resp. Failure

2) ECG → M/c → Tachycardia, T wave inversion $V_1 - V_4$

3) Most specific → S, Q_3, T_3 pattern. → massive PTE

4) CXR → N M/c
FOCAL OLIGEMIA
(Westermark Sign)



2) Wedge shaped deformity above diaphragm
Hampton's hump 181

3) Palla's sign - Dilatation of R Descending Pul. artery

D-Dimer :-

Fibrin Degradation product

Elevated in PTE

Sensitive not specific

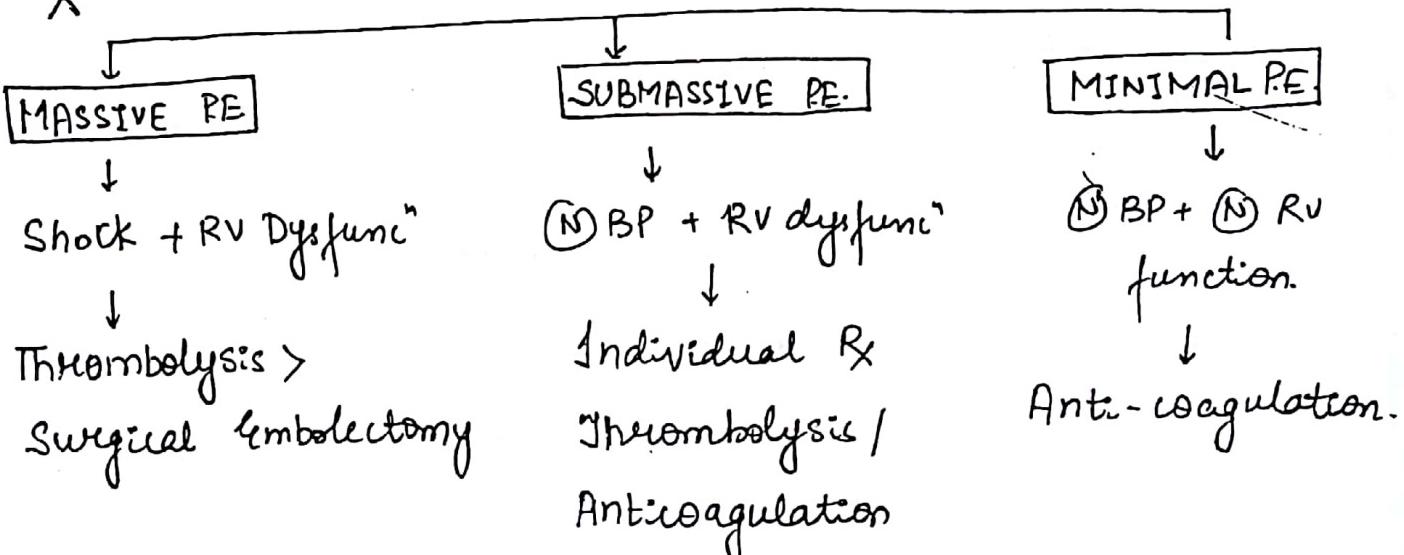
poor predictive value but good neg. predictive value

5) Ioc \Rightarrow CT Palm. Angio

6) Gold Std \Rightarrow Invasive Pul angiography

7) V/P scan. - outdated $\xrightarrow{\text{♀}}$
 $\xleftarrow[\text{in}]{\text{used}}$ Contrast intolerance.

Rx



PULMONARY HTN

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MPAP $> 25 \text{ mmHg}$ @ rest

MPAP $> 30 \text{ mmHg}$ \cong exercise

MECH. WHO CLASSIFICATION

Group I - Direct involvement of Pul. artery

a) Heritable cause/ 1^o Pul HTN - mutation in BMPR₂

↑ smooth m/c proliferation

↓
young ♀.

Biopsy \rightarrow Plexiform lesion,

b) Connective Tissue Disease

M/c cause is Scleroderma, SLE.

c) Drugs/Toxin - Fenfluramine.

Toxic rapeseed oil

Group 2 - Due to L Heart Disease

Group 3 - Due to Rep. diseases.

COPD / ILD / Bronchiectasis / OSA

Hypoxemia \rightarrow Pulm. vasoconstriction \rightarrow P. HTN \rightarrow Cor Pulmonale

Group 4 - Due to chronic thromboembolic events in Pulm. circulation.

Group 5 - Miscellaneous / unclear cause

Sarcoidosis

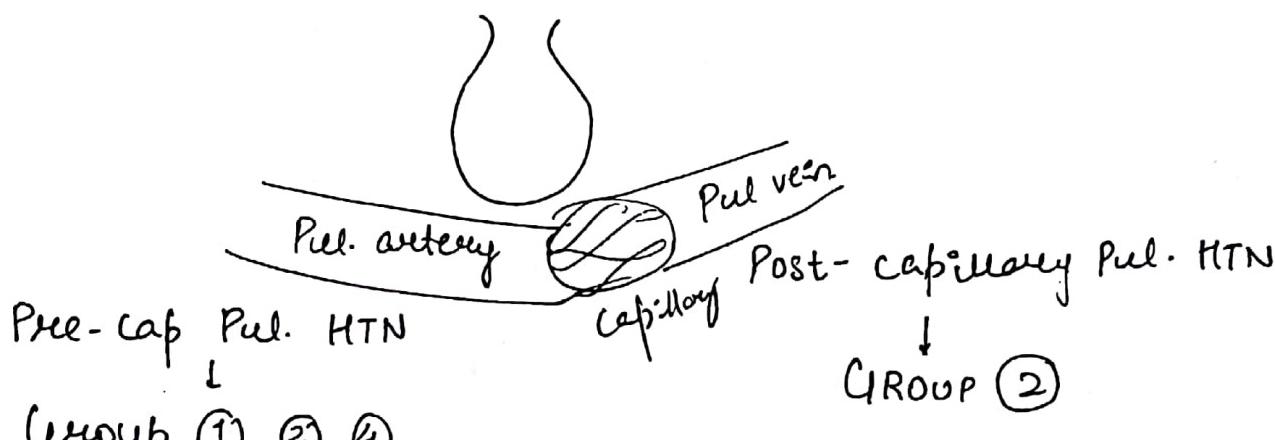
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Sickle cell Disease

Langerhans cell histiocytosis / eosinophilic

Lymphangiomatosis granuloma
↓
(misnomer)

Lymphangiomyomatosis



Group ①, ③, ④

MPAP \geq 25 mm Hg

MPAP $>$ 25 mm Hg

PcWP $<$ 15 mm Hg

PcWP $>$ 15 mm Hg

Rx

GROUP ① & Refractory
cases from other groups

Other Groups
Rx underlying disease

1) CCB - Nifedipine (now not
used)
frequently)

2) PDE 5 Inhibitor

Sildenafil
Tadalafil

3) Endothelin Receptor Antagonist
Bosentan
Ambrisentan.

- 4) Prostacyclin -
 Epoprostenol (IV)
 Fluprostan (Inhaled)

- 5) Guanyl cyclase activators
 Riociguat

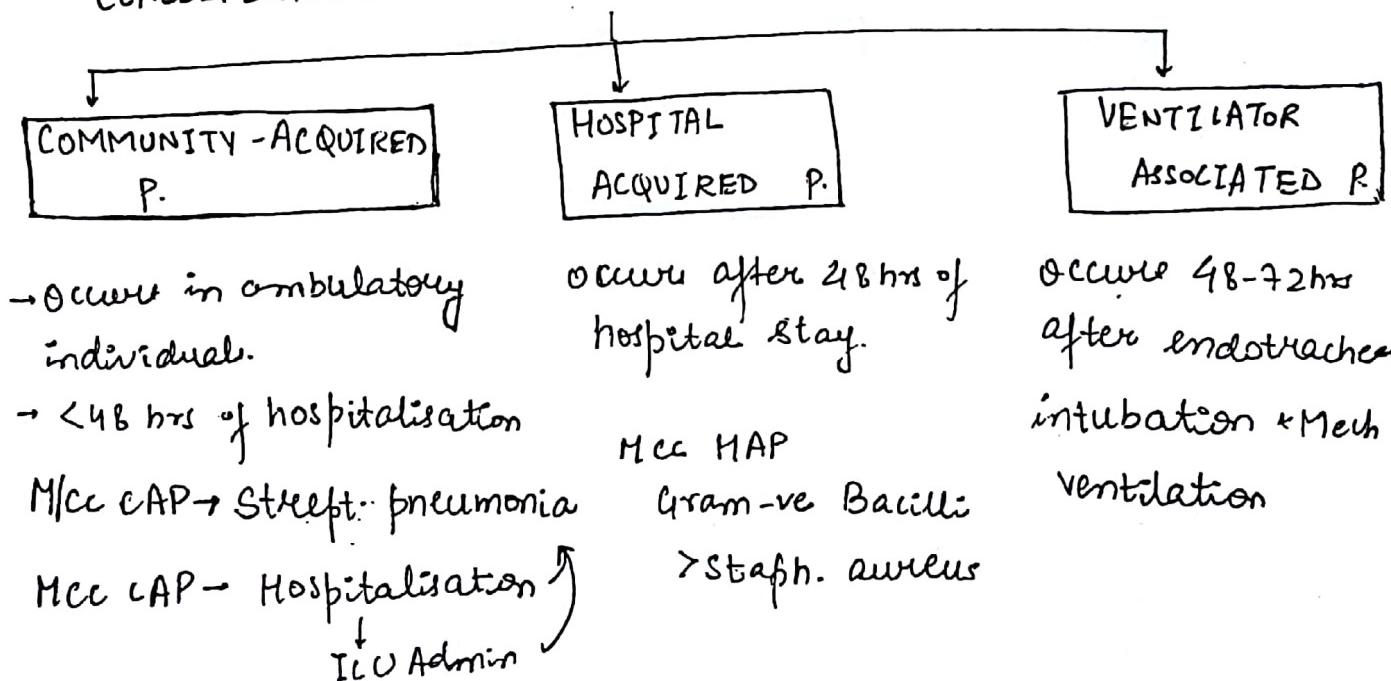
Doc for Low Risk Cases :- Initial monotherapy of Less symptoms either PD5 Inhibitor or ETRA
 followed by combination Rx.

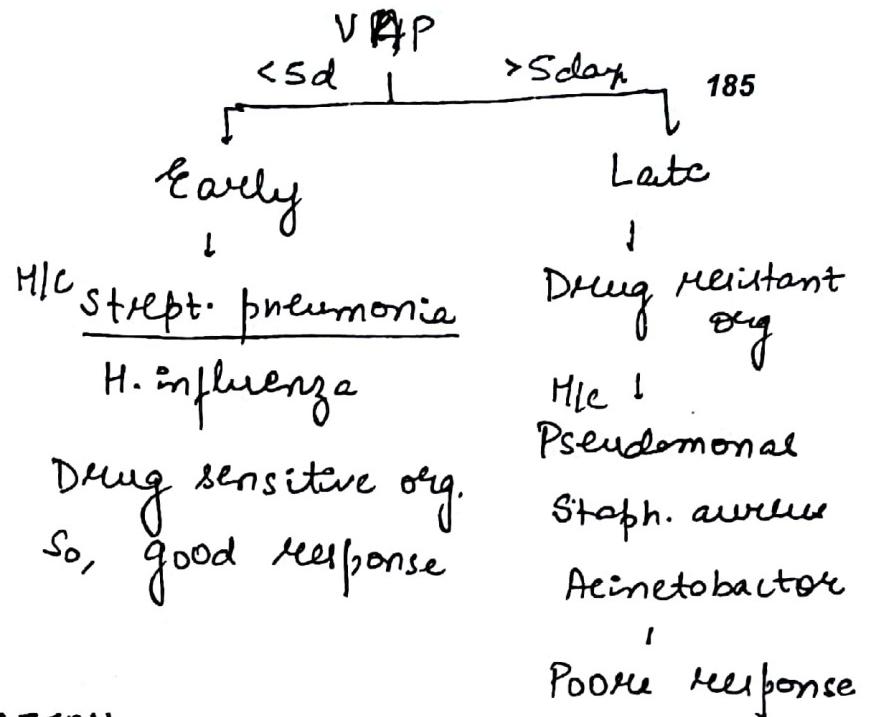
Doc for High Risk / Emergency - Prostacyclins (Symptoms at Rest)

PNEUMONIA

Acute resp. illness characterised by Radiological Pulmonary shadowing.

CLASSIFICATION -





CLINICAL CLASSIFICATION

TYPICAL



- Fever + Productive cough
- Predominant neutrophilic leucocytosis
- Gram staining → reveal organisms

CXR → Alveolar exudate

MIC - Strept. Pneumoniae
Staph. aureus
Klebsiella
Pseudomonas

ATYPICAL



Interstitial Inflammation

- Fever + cough → scanty sputum
- Mild Leucocytes
- Gram staining → no organism

CXR - NO alveolar exudate
→ Interstitial pattern

MIC - Mycoplasma
Legionelle
Coxiella
Chlamydia
Viral Pneumonia

TYPICAL PNEUMONIA

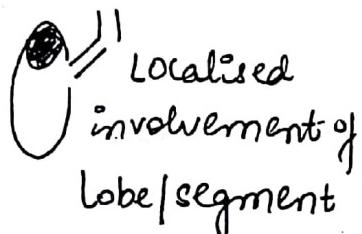
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(I) STREPT

Risk Factors } M/c -
Smokers
alcoholics
DM

c/F Red Musty sputum

CXR



M/c pattern in CAP

Rx - β Lactam

(IV) PSEUDOMONAS

→ Frequently occurs as VAP

→ occurs as Recurrent pneumonia in

structural
Lung disease
→ cystic fibrosis
Bronchiectasis

→ Fever, mucopurulent secretion,
Leucocytosis.

(II) STAPH

IV drug user
pneumonia

Fatal pneumonia post
viral illness

mucopurulent sputum

CXR



B/L, patchy
involvement

M/c pattern in nosocomial
Pneumonia

Pneumatocele + cavity +
Lung abscess. may be
seen

Rx MRSA = Vancomycin

VRSA = Linezolid

Red currant
Jelly sputum

CXR



Bulging fissure
sign

- cavities
- Dense consolidations
- Lower lobe
involvement
seen if
hematogenous
spread

Rx -

β Lactam +
Aminoglycoside

(III) KLEBSIELLA

Alcoholics
DM
malnourished



CXR

Bulging fissure
sign

- cavities
- Dense consolidations
- Lower lobe
involvement
seen if
hematogenous
spread

- B/L infiltration of CXR

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Rx - Two Antipseudomonal ABs of 2 different classes.

Antipseudomonal ~~AB~~ β -lactam + FQ (or) Aminoglycoside

ATYPICAL PNEUMONIA

MYCOPLASMA / Walking P.

M/c atypical pneumonia

Eaton agent pneumonia

Man \rightarrow Man transmission.

Extrapulmonary features

1) CNS - GBS
peripheral neuropathy

2) Ear - Bullous myringitis

3) Blood - \uparrow cold agglutinins
Haemolytic anaemia

4) CVS - Myocarditis
Pericarditis

5) SKIN - Erythema Nodosum

No cell wall (+)

Rx - β -Lactam / FQ / Tetracycline

LEGIONELLA

M/c mode of transmission -
micro aspiration $>$ aerosolization

Spreads through contaminated water

Limited man to man transmission
Special Features :-

1) Associated GI features: diarrhea

2) " CNS features:-

confusion, headache,
high grade fever

3) Altered LFTs

4) $\text{S-Na}^+ < 130 \text{ meq}$

Gram staining \rightarrow no organism

Poor response to β -lactams

old age, immunocompromised

occurs \sim in 10 days discharge
from hospital

Rx - β -FQs / Macrolide / Tetracycline

Resp FQs - Levoflo/Moxi

PNEUMOCYSTIS PNEUMONIA (PCP)

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H/c opportunistic infection in HIV = TB

H/c pneumonia in HIV = TB

H/c pleural effusion in HIV = TB

H/c fungal pneumonia in HIV = PCP

R/F:-

- 1) CD₄ < 200 / μL in HIV
- 2) Long Term Immuno suppressive Rx
- 3) Organ Transplant
- 4) 1° Immuno compromised

C/F:-

Subacute onset

Fever

Shortness of Breath

Hyoxemia

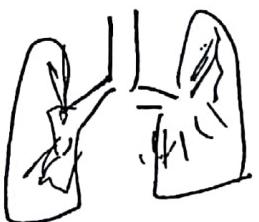
CXR:-

Perihilar infiltrates

Diffuse interstitial infiltrate

In few - pneumatocele

Complicate as Pneumothorax



Δ :- Visualize the cyst

Wright-Giemsa

Komori-methamine stain.

Broncho-alveolar lavage (Best sample)

Rx - COTRIMOXAZOLE (Septrex)

- If sulphur allergy →
- 1) Clindamycin + Primaquine
 - 2) Trimethoprim + Dapsone
 - 3) Pentamidine
 - 4) Atovaquone

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DOC for Prophylaxis → COTRIMOXAZOLE

↓

DOC for NOCARDIOSIS.

VIRAL PNEUMONIA

BIRD FLU (H_5N_1)

SWINE FLU (H_1N_1)

- Avian Influenza

- ↑ M → M transmission

- Less M → M transmission

- Epidemic + Pandemic

Epidemic not pandemic

DOC - oseltamivir

DOC - oseltamivir

75mg BD for 5 days

(neuramidase Inhibitor)

Doc prophylaxis - oseltamivir

75mg OD for 10 days

other drugs - Zanamivir
Peramivir

ASSESSMENT of SEVERITY

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Confusion

Urea $> 7 \text{ mmol/L}$ or $> 20 \text{ mg}$

RR $> 30/\text{min}$

B - SBP $< 90 \text{ mm Hg}$ DBP $< 60 \text{ mm Hg}$

65 Age age > 65

0-1 \Rightarrow Home Rx & Antibiotic

2 \Rightarrow Hospitalization + Rx

3-5 \Rightarrow Consider as severe pneumonia, may require ICU admission.

EMPIRICAL REGIMEN FOR HOSPITALISED Pt OF PNEUMONIA



TYPICAL

+

ATYPICAL

β lactam

+

Macrolide

LUNG ABSCESS

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1° ABS form

M/c type

Due to aspiration

M/c org anim - oral anaerobes

↓

Rx - IV. Clindamycin.

2° form

Occurs due to pre-existing disease process in lung

Bronchial obstruction

Immune deficiency

Staph, Klebsiella

Rx = Broad spectrum ABs

Strategies to Prevent VAP :-

- 1) Elevation of Head of Bed. 30°-45°
- 2) Oral Decontamination w/ Chlorhexidine
- 3) Sedation vacation (1 sedation)
- 4) Assessment of readiness to extubate daily
- 5) Use of NIV wherever feasible

X Frequent change of Tube X

ORAL ANAEROBES -

- Peptostreptococci
- Fusobacterium
- Bacteroides

PLEURAL

EFFUSION

192

↓
TRANSUDATE (M/Lc)

LIGHT's CRITERIA

EXUDATE

Ple. fluid. Protein < 0.5
S. protein

Ple. fluid LDH < 0.6
S. LDH

Cause -

- 1) CHF (M/Lc overall)
- 2) Hepatic Hydrothorax
- 3) Nephrotic Sx

$> 0.5, 0.6$

Cytology = ? malignant cells

Cell count

Gram staining = ? infection

TB marker = ADA,
Interferon γ

Special Features

1) Low glucose ple. fluid ($< 60 \text{ mg}/\text{dL}$)

- a) Empyema
- b) Malignancy
- c) RA
- d) TB (Hansen)

2) High Amylase

- a) Pancreatitis
- b) Oesophageal rupture
- c) Malignancy

3) High Lipid Ple. Eff / white coloured

↓
Chylothorax

PL TGA $> 110 \text{ mg}/\text{dL}$. Chyle due to disruption
of thoracic duct
H/C - Surgical Trauma
Malignancy

↓
Pseudochylothorax

Accumulation of
cholesterol crystals
in long standing eff.
TB, RA, ch. empyema,
myxoidema
Cholesterol $> 200 \text{ mg}/\text{dL}$.

* Parapneumonic eff

M/c of exudative pleural eff

eff associated w/ Pneumonia
Bronchiectasis
Lung abscess

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[Milky white BAL
Alveolar Proteinosis]

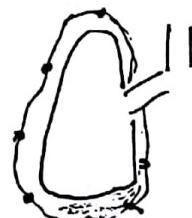
Indications of ICD insertion in parapneumonic eff :-

- 1) Pus in pleural cavity
- 2) pH < 7.2 (pleural fluid)
- 3) Ple f. glucose < 60mg%
- 4) Loculated pleural effusion
- 5) Gram staining reveals organisms

TB Effusion

- M/c exudative effusion in India

- Occurs due to hypersensitivity
Response to TB Bacilli in
Pleural Tissue



- Exudative → Lymphocyte predominant

ADA > 40 IU

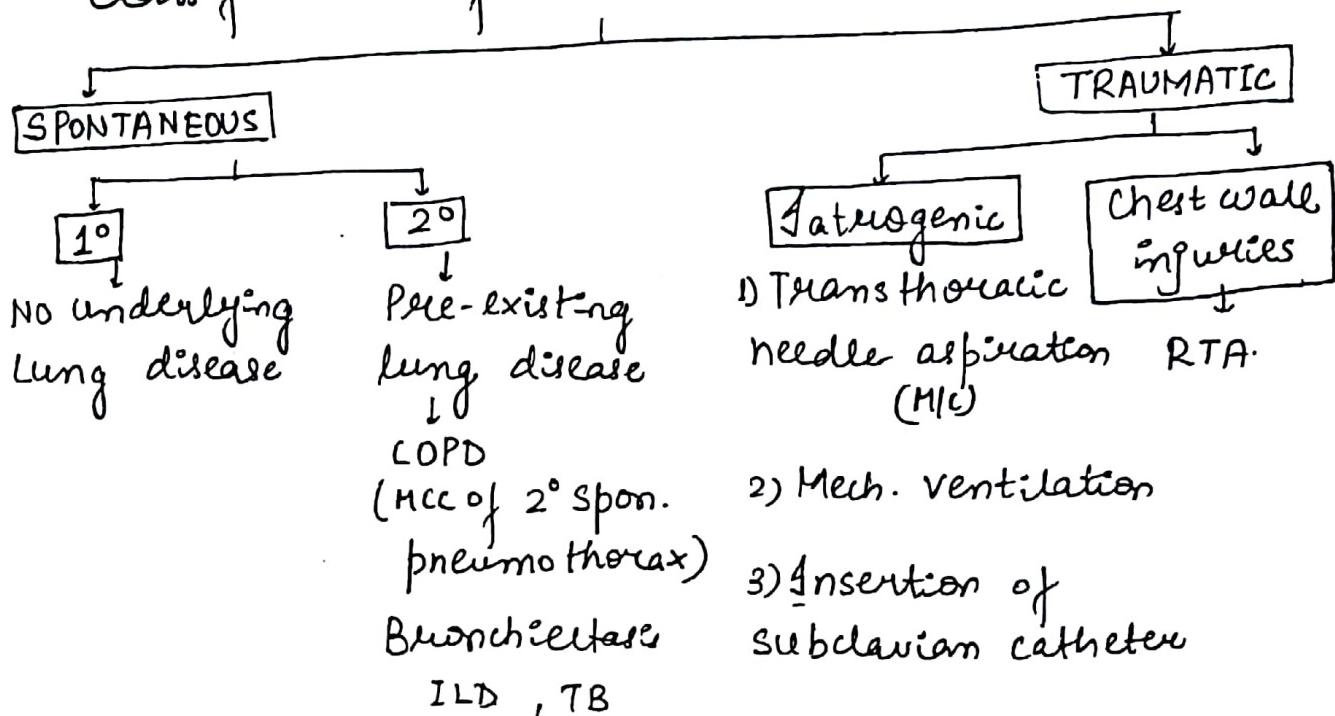
IFN Y > 140 pg/mL

↓ mesothelial cells

- Pleural fluid for AFB only positive in 20-30% cases.

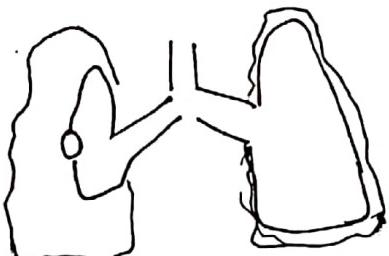
Gold Std - Thoracoscopic pleural biopsy + Culture for M. tb.

Classification of Pneumothorax :-



TENSION PNEUMOTHORAX

- 1) Large air leak
- 2) Air leak serves as ball valve (or) one way valve mechanism



- 3) ↑↑ Positive intrapleural Pressure
- 4) Compressing adj lung + mediastinal vessels

↓
↓ VR

↓
shock (medical emergency)

- 5) Rx - Next step / Best step - Insertion of wide bore needle
 - ② 2nd I.c.s. anteriorly mid clavicular line on affected side followed by JCD insertion.

High Inspiratory Pressure alarm on ventilator suggest ~~Po~~ Tension Pneumothorax.

Pneumo Mediastinum

Air in mediastinum

C/F - Shortness of Breath
Chest pain

HAMMAN's Crunch → Crunching sound synchronous with heart beat

CXR - Continuous Diaphragm Sign.
Subcutaneous Emphysema

ASTHMA

Characterised by recurrent symptoms due to variable & reversible bronchoconstriction caused due to airway hyper-responsiveness to variety of stimuli

COPD - characterised by persistent symptoms & airflow limitation due to airway & alveolar abn caused by significant exposure to noxious stimuli.

ASTHMA

Allergen related
Reversible airflow limitation
Early presentation
Relief in Bronchodilators

COPD

Smoking related
Persistent airflow limitation
Delayed presentation
only partial response

TYPES PATHOGENESIS

EXTRINSIC / ATOPIC / ALLERGIC

Allergen related

S-IgE ↑

Skin test +ve for allergen

Mild form

Young onset

H/c allergen world

↳ HOUSE DUST MITE / Dermatophagoides

Pollen → cause Thunderstorm

Asthma

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INTRINSIC / NONALLERGIC
NONATOPIC / IDIOSYNCRATIC

Viral infection ⇒ Trigger

S-IgE N

Skin test -ve for

Severe forms

Late onset

Δ :-

1) SPIROMETRY

obstructive

Bronchodilator reversibility = $\uparrow \text{Fev}_1 > 12\% \text{ (or) } 200\text{cc}$
after SABA.

$\text{Fev}_1 65\% \xrightarrow[15\text{ min}]{\text{SABA}} \text{Fev}_1 80\%$

2) PEFR Variability

>20% diurnal variation.

3) METH. CHOLINE challenge Test / Broncho provocation Testing

fall in $\text{Fev}_1 > 20\%$ after meth. choline.

for airway hyper-responsiveness

4) $\text{FeNO} > 50 \text{ PPb}$ ≈ eosinophilic inflammation.

ACUTE SEVERE ASTHMA

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C/F -

- 1) Pt. speaks in words
- 2) Can't recline
- 3) RR > 30/min
- 4) HR > 120/min
- 5) B/L Wheeze
- 6) Accessory muscle use

7) Pulse Paradoxus. → [Rapid change in intrapleural pr.]
causes this.

Functional Parameters :-

- 1) PEFR < 50% predictive value
- 2) $\text{SpO}_2 < 90\%$
- 3) $\text{PaO}_2 < 60 \text{ mmHg}$

→ Type I Resp. Failure

→ Type II RF can occur in severe cases

↳ due to fatigue of resp. muscles.

* Life Threatening Asthma :-

- 1) Patent - altered sensation
- 2) Silent chest
- 3) ↓ Respiratory effort
- 4) $\text{PaO}_2 < 60 \text{ mmHg}$
- 5) $\text{PaCO}_2 \uparrow \uparrow$

Rx - 1) $O_2 +$

2) SABA + (Salbutamol) + Inhaled corticosteroid
· SAMA (Ipratropium)

2) I.V. Steroid

↳ ↓ Inflammation

↳ ↑ sensitivity of β_2 receptor to broncho dilator

3) Theophylline now not used routinely

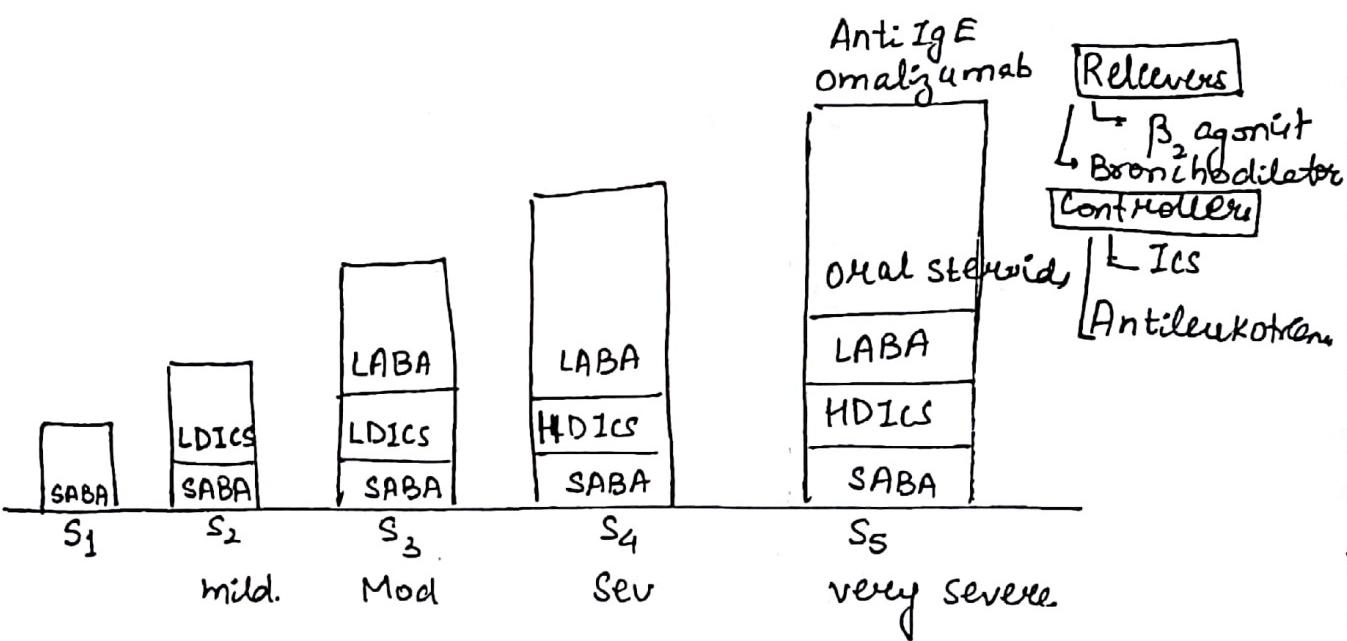
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4) In few cases IV MgSO_4 given

5) In deteriorating / life threatening cases \Rightarrow **Invasive Mech. ventilation.**

High inspiratory flow \leftarrow
 \rightarrow Expiration Time
 $I:E = 1:3 \text{ or } 1:7$

Step Wise Therapy & Classification	Persistent			
	Intermittent	Mild	Mod	Sev
Day time sx	< 2/week	> 2/week	daily	throughout day
Night time awakening	< 2/month	> 2/month	> 2/week	daily



LDICS \rightarrow low dose ICS.

HDICS \rightarrow High dose ICS.

Most imp. in asthma management is pt. self education & active self Mx. 199

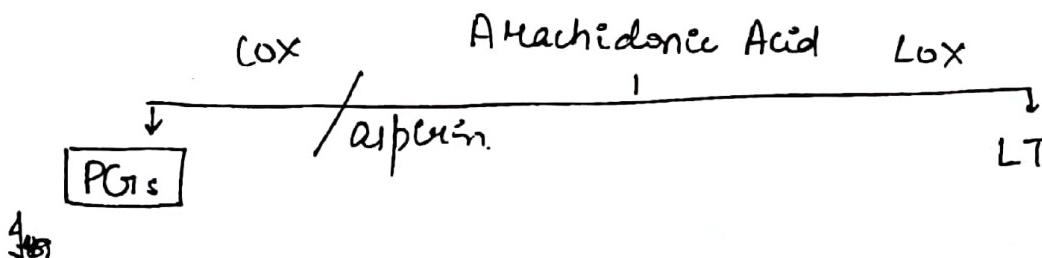
EXERCISE INDUCED ASTHMA

In susceptible individuals, exercise can induce asthma more frequent during cold & dry climate \rightarrow hot humid condition.

Doc for short term prophylaxis = SABA \rightarrow Anti-leukotriens / Mast cell stabilizers.

Doc for Long term prophylaxis & corticosteroids
overall control of disease]

ASPIRIN INDUCED ASTHMA



Samter's TRIAD-

Nasal polyposis + Aspirin sensitivity + Asthma

In susceptible individuals, aspirin blocks Cox pathway & shifts balance towards Lox pathway \Rightarrow ↑ LTs

↓
Bronchospasm-

Rx = ICS + Asptc. SABA + Anti-leukotriens + Aspirin desensitization.

BRITTLE ASTHMA

Unstable Disease \in frequent exacerbations

(N)

Lung function

Type 1 Brittle

Persistent fluctuation
in lung functions



Difficult to Rx asthma

* Oral corticosteroids
+ continuous infusion =
 β_2 agonist

Type 2 brittle

Near normal lung
function → Rapid
fall + death.



Localised anaphylaxis

Laryngospasm

DOC :- Subcutaneous
Epinephrine +
Adrenaline

CORTICOSTEROID RESISTANT ASTHMA

Poor response to Rx after 2 weeks of oral cortico-
steroids (40mg/day) Rx

steroid sparing drugs can be used.

Anti IgE = Omalizumab

Anti IL5 = Mepolizumab

COPD

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(HR. BRONCHITIS:-

Cough & sputum for >3 months in 2 consecutive years

EMPHYSEMA:-

"Destru" distal to terminal bronchiole.

R/F:-

- 1) Smoking
- 2) α_1 AT Deficiency
- 3) Indoor + outdoor pollution.
- 4) Coal exposure

②

- young age
- Less smoking H/o
- Family H/o - Chr. 14, AR.
- B/L Lower predominant
- Bronchiectasis
- Unexplained Liver Disease.

TYPES OF EMPHYSEMA

CENTRI ACINAR

occurrence Smokers
M/c overall.
Upper lobes

Pathology



RB involved
alveolar duct +
Sac spared

PANACINAR

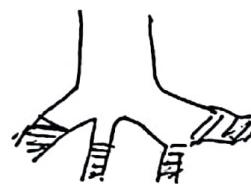
α_1 AT Def.
More severe in
LL



Resp. Bronchiole +
Alv. Duct + Sac
involved

DISTAL ACINAR

Adjacent to peracute
foci.
upper $\frac{2}{3}$ rd of Lung



Resp. Bronchiole spared
Alv. duct + Sac
involved

A: → SPIROMETRY

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$$\frac{FVC}{FEV_1} < 0.7 \approx \text{obstructive}$$

no significant Bronchodilator reversability

GOLD Staging (Global Initiative for Obstructive Lung Disease)

I Mild $FEV_1 / FVC < 0.7$ $FEV_1 \geq 80\% \text{ Pred. } FEV_1$

II Mild. " " " $FEV_1 [50-79\%]$ " "

III Severe " " " $FEV_1 [30-49\%]$ " "

IV very severe. " " " $FEV_1 < 30\% \text{ pred. value}$

Prognosis Index

BMI

Obstruction (FEV_1)

Dyspnoea (MRC scale)

Exercise Capacity \Rightarrow Distance covered in 6 minute walk test

Low score \Rightarrow Good Prog.

High score \Rightarrow Poor Prog., ↑ mortality

CHARACTER

BLUE BLOATER

PINK PUFFERS

PATHOLOGY

Chronic Bronchitis.

Emphysema.

SYMPTOM

Cough = expectoration

Shortness of Breath

APPEARANCE

obese + comfortable at rest

Lean + tachypnoeic at rest

POSTURE

Breath sounds

Rhonchi - Noisy

Less noisy
Hyperinflated Lung
obstructive

CXR

↑ Interstitial markings
obstructive

Rx :-

1> Smoking cessation. → most imp. intervention.

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2> BRONCHODILATORS

a) LABA

ultra LABA → O.D. Dose

- ✓ Indacaterol.
- ✓ Vilanterol
- ✓ Olodaterol

b) LAMA

Tiotropium

Umidilnidium

Glycopyronium.

3> STEROID :-

a) Inhaled

↓ freq. of exacerbation

b) Systemic

During exacerbation.

4> SELECTIVE PDE₄ INHIBITOR:-

Roflumilast

5> ANTI BIOTICS :-

During exacerbation (H. influenza)

6) MUCOLYTICS -

N Acetyl cysteine

7) If Hypoxemia → Long term O₂ therapy (15 hours a day)
low flow O₂

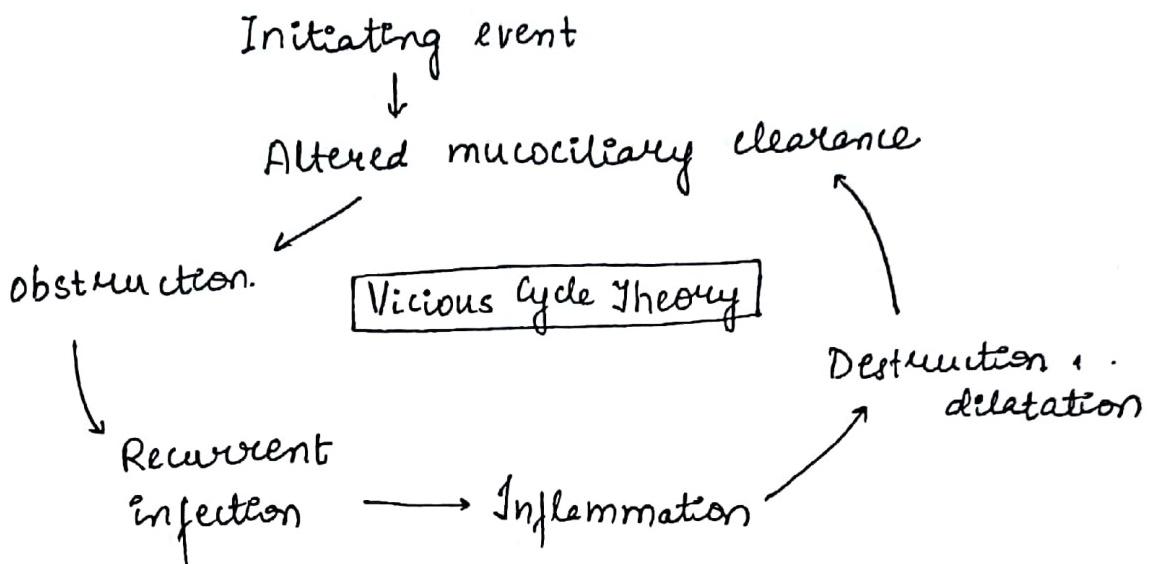
8) Lung volume Reduction Surgery

9> LUNG TRANSPLANTATION (M/c indication for lung transplantation
is COPD)

10> During exacerbation, 1st choice → non-invasive ventilation.
> invasive →

BRONCHIECTASIS

Ab N Permanent Dilatation of bronchi due to loss of muscle & elastic tissue.



C/F :-

copious sputum
coarse crepts

ETIOLOGY & MECH :-

I) BRONCHIAL OBSTRUCTION

a) **Intramural**



Tumours - Carcinoïd

Sq. cell carcinoma

Small cell carcinoma

b) **Extrinsic compression.**

Enlarged TB hilar LN can compress R middle lobe.

Bronchus → R middle lobe collapse + bronchiectasis

↓
BROCK's SYNDROME.

II> BRONCHIAL INJURY

A) Infection

TB, adenovirus

B) ²⁰⁵ Altered Immune response

→ Connective Tissue disorder

→ Allergic Bronchopulmonary Aspergillosis (ABPA)

III> TRACTION BRONCHIECTASIS in ILDs.

IV> GENETIC CAUSES

A) 1° ciliary dyskinesia

B) cystic fibrosis

C) Cartilage Defect

William Campbell S., Mounier Kuhn syndrome

D) Yellow Nail Syndrome

Long. Lymphoedema + Yellow nail + Pleural Effusion
+ Bronchiectasis

CYSTIC FIBROSIS

Inheritance - AR

Chromosome 7q

Gene - CFTR

Channel - Cl⁻

Mutations - Class I - VI

Mc class II, ΔF508

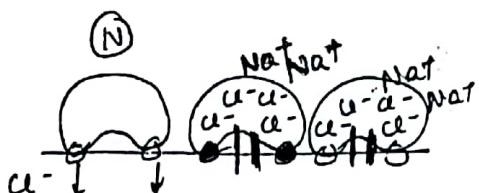
" Thick secretions "

(I)

Resp. Tract

GRT

Reproductive Tract



watery secretions Thick viscous secretions
dehydration

ENac → responsible for pathophysiological process

(II)

Sweat Gland



SCREENING Test
↑ Sweat Cl- > 60 mg/dL

Other Inv:-

- 1) DNA analysis for mutations
- 2) ↑ Nasal Potⁿ Difference
- 3) CFTR Gene Sequencing :- Gold Std.

SYSTEMIC MANIFESTATIONS:-

1) Respiratory Tract -

URT
↓Recurrent infections
Sinusitis

LRT

↓

Recurrent pneumonia
(M/c pseudomonas), steph.
Bronchiectasis, Lung abscess
Emphyema, P. thrombosis,
Resp. failure, Hypoxemia,
P. HTN, Cor Pulmonale

2) GIT

neonate Meconium ileus.

Liver → Biliary cirrhosis,

GB - Gall stone

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Pancreas

- Endocrine insufficiency - early manifestations
- DM, → occurs later.

3) Reproductive Tract -



In utero occlusion of vas Deferens
by thick secretions → AZOOSPERMIA.
↓
infertile

Rx

1) CFTR Modulators :-

Ivacaftor - G551D mutation class III

Lumacaftor + Ivacaftor - tried in class II

TYPES OF BRONCHIECTASIS -

(N)



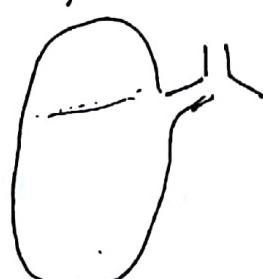
H/C-Cylindrical

Varicose

Saccular

SITES of BXIS -

1) Upper Lobe



1) Cystic fibrosis

2) TB

3) Post radiation BXIS

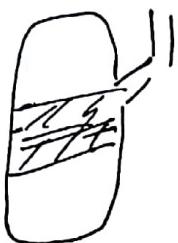
2) Lower Lobe



- 1) Interstitial Lung Disease
- 2) Ch. recurrent aspiration
- 3) Immunodeficiency state

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3) Middle Lobe - non-tubercular mycobacterium.



Mycobacterium avium complex (MAC)

Rx of B'XIS-

1) Airway clearance.

Mucolytics

Chest Physiotherapy.

2) Antibiotics

During exacerbation

Prophylaxis

Long term
Azithromycin
(6 months)

Inhaled
Tobramycin
(1 month on-off)

3) Bronchodilator ICS beneficial in some

4) If Hypoxemia \Rightarrow O₂.

5) Localized Disease \rightarrow Sx

6) Diffused " \rightarrow Lung Transplantation.

High flow O_2 not recommended. Y?

1) Abolition of Hypoxemic resp. drive

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2) High O_2 given can cause release of CO_2 from RBC

↳ HALDANE

EFFECT.

IOC :- HRCT Chest

EOSINOPHILIC LUNG DISEASES

[Peripheral eosinophilia + Lung infiltrates]

CLASSIFICATION

Unknown cause

Known cause

1) Acute eosinophilic pneumonia

1) PARASITIC INFESTATIONS
(nematodes)

2) Chronic " "

Loeffler's pneumonia

3) Hypereosinophilic Syndrome

2) ABPA

4) Churg Strauss Sx

3) Drugs:-

Nitrofurantoin

Sulfonamides

Isoniazid

Pencillamine

Hypereosinophilic Syndrome-

Persistent eosinophilia $> 1500/mm^3$.

+ end organ infiltration.

CHARACTER

Ac. EP

Ch4. E.P.

Smoking H/o

+++, new onset smokers

±

Asthma H/o

--

++

C/F - Radiology

Acute shortness of Breath
+ Hypoxemia +
B/L diffuse infiltrates.

Cough + wheeze.
Peripheral opacities

Peripheral eosinophilia

Initially not seen but seen
during later course of disease

Usually seen

	AEP	CEP
BAL eosinophilia	BAL > 25% eosinophil	BAL > 40% eosinophil
Rx	Steroid	Steroid

ASPERGILLUS & LUNG

I> HYPERSENSITIVITY RxN. → DOC + steroid

Type I



Asthma

Type I, III, IV



ABPA

II> PNEUMONIA IN IMMUNOCOMPROMISED → DOC + VORICONAZOLE.

= Invasive Aspergillosis

Trans bronchial angio invasion. → may develop hemoptysis.
Fever + SOB.

DOC for I ~~+~~ ⇒ STEROID.

DOC for II ⇒ VORICONAZOLE

III> COLONISATION IN PREEXISTING LUNG CAVITY

Aspergilloma / Fungall BALL

CXR → Air crescent sign.

⇒ Ball changing its position in decubitus.



Rx - Resection of pt. in symptomatic

CRITERIA FOR ABPA

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- 1) Predisposing cond' -
 - Asthma
 - Cystic Fibrosis
- 2) Peripheral **eosinophilia**
- 3) S-IgE → **> 1000 IU**
- 4) Aspergillus specific IgE + IgG will be +ve
- 5) Skin test +ve **Aspergillus fumigatus**
- 6) CXR - **fleeting opacities** → upper zone
- 7) Central (or) Proximal **B' XIS**.

Doc:- Systemic Steroids.

CT Chest -

- Finger in glove
- Toothpaste

HYPERSensitivity PNEUMONITIS

or Extrinsic Allergic Alveolitis

Type III + IV HSN

S-IgE → **N**

No. peripheral eosinophilia

BIOPSY → non caseating granuloma + cellular bronchiolitis + Interstitial inflammation.

Eos.

DISEASE	EXPOSURE	ANTIGEN
1) Farmer's Lung	Moldy hay	Microsporidia fungi
2) Bagassosis	Sugarcane dust	Thermoactinomyces sacchari
3) Bird fancier Lung	Pigeon excreta	Avian protein
4) Malt worker lung	Mouldy Barley	Asp. clavatus
5) Hot tub lung	Contaminated water	Non-Tubercular mycobacterium

Diagnostic CRITERIA :-

- 1) Exposure to known antigens.
- 2) Presence of serum precipitins against offending Ag.
- 3) Occurrence of symptoms \leq in 4-6 hrs of exposure
- 4) Recurrence of symptoms on exposure
- 5) Inspiratory crepitaculation.
- 6) wt. loss

TYPES

	CT. Chest
ACUTE - hours to days	Ground glass opacities
SUBACUTE - week.	Centrilobular nodules
CHRONIC - Month	Fibrosis (upper zone)

Rx - Most Important \rightarrow Avoidance of allergen.
Systemic steroids

ILD

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Defn:- Group of Disorders characterised by predominant involvement of interstitium progressing to fibrosis & vary in mechanism & magnitude.

ETIOLOGY:-

I) Inhalational ILD

Organic Dust

Hypersensitivity
Pneumonitis

Inorganic Dust

Silica
Asbestosis

II) Drugs/ Radiotherapy

Amiodarone
Methotrexate
Busulfan

III) Connective Tissue Disorder

Scleroderma
RA
SLE

IV) IBDs

V) Infection - TB

VI) Malignancy

VII) Sarcoidosis

VIII) Idiopathic

PATHOLOGICAL PATTERNS:-

I) Usual Interstitial Pneumonia (UIP)

2) Non-specific " " (NSIP)

3) Acute Interstitial Pneumonia (AIP)

- 4) Cryptogenic Organizing pneumonia (COP)
 5) Respiratory Bronchiolitis (RBILD)
 6) Desquamative Interstitial Pneumonia (DIP)
 7) Lymphocytic " (LIP)

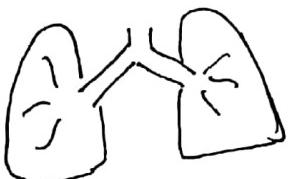
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IOC: CT HRCT chest

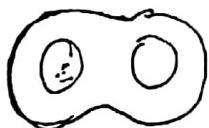
Confirmatory Test: Surgical Lung Biopsy

RADIOLOGIC PATTERNS

Reticular Pattern.



CT Chest



Mild opacity = Ground Glass opacity



↑ sed density = consolidation.

↓ Fibrosis



TRACTION
B^oXIS

fibrosis + nt
↓ Lung volume



Honey combing

subpleural involvement
(near to pleura)

M/C
form
usual Interstitial Pneumonia
or Idiopathic Pul. Fibrosis

C/F. 50-60 yrs ♂ > ♀, Smoker.
insidious,
Auscultation - inspiratory crept.
exam - clubbing

Biopsy Heterogeneous involvement
Fibroblastic foci

Radiology - B/L Lower zone &
- subpleural involvement
- Minimal Ground glass
opacity
- Significant Traction Bi'sis
- Honey combing

Rx + Prognosis Poor response
to Pirfenidone
Nintedanib

NSAJP. (M/c form of
connective tissue
disorder associated
ILD)

40-50 yrs ♀ > ♂
Non-smoker, subacute onset.

No fibroblastic foci
Lymphocytic inflammation

B/L ground glass opacities
Minimal Traction Bronchiectasis
Rare honey combing

Good response to
steroid

ACUTE INTERSTITIAL PNEUMONIA / HAMMAR RICH SYNDROME

Pt - present w/ acute SOB + Hypoxemia + Diffuse infiltrate
Idiopathic ARDS

Rx - supportive. High mortality

CRYPTOGENIC ORGANISING PNEUMONIA / BRONCHIOLITIS OBLITERANS ORGANISING PNEUMONIA (BOOP)

- 1) Pneumonia like illness
- 2) Proliferation of granulation tissue in airway =>
MAISON BODIES

3) Presence of Interstitial infiltrate.

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CXR :- Bl Peripheral Consolidation.

Rx :- STEROID.

SMOKING AND ILDs

Resp. Bronchiolitis associated ILD

Desquamative Interstitial Pneumonia

Adult Pulmonary Langerhans cell histiocytosis

Acute eosinophilic pneumonia

Pulmonary haemorrhage syndromes

Idiopathic pulmonary fibrosis

ILDs Less Prevalent In Smokers :-

1) Sarcoidosis

2) Hypersensitivity pneumonitis

SARCOIDOSIS

Multisystem Disorder characterised by non-caseating Granuloma.

Etiology :- , Autoimmune

2) Propriobacterium

3) Mycobacterium

4) unknown.

5) Genetic susceptibility - HLA DRB₁, 1101

M/c → Pul. Involvement.

Scadding Staging I- Hilar adenopathy



2/7

II- LN↑ + Lung infiltrates



III- Lung infiltrates alone



IV- Fibrosis



Upper zone predominant Disease

PHENOTYPES

1) LUPUS PERINIO-

Cutaneous involvement → Bridge of nose
area beneath eyes + cheeks

2) LOFGREN SYNDROME-

Erythema nodosum, Hilar LN↑
Uveitis (MC - Anterior), Arthritis

3) UVEO-PAROTID FEVER

Uveitis + Parotiditis + Fever + CN 7th Palsy

4:-

1) → release ACE. + $1,25(\text{OH})_2 \text{ VITD}$

Non-caseating
granuloma

TS · ACE > titer (N)

Hypercalcemia

2) Blood :- Peripheral lymphopenia - sequestration of lymphocytes
into lung

3) Bronchoscopy :-

BAL - Lymphocytes $\frac{\text{CD}4}{\text{CD}8} \uparrow$

4) Biopsy - Non-caseating granuloma

TOC → Incomparable clinical scenario ⇒ Biopsy of involved organ.
Showing non-caseating granulomas is S/O sarcoidosis

57 CT chest → Lung infiltrates
LN ↑

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In TB LN → Caseating ⇒ central hypodensity = peripheral rim enhancement

Sarcoidosis → uniform density

67 Gallium Scan

a) ↑ uptake by Parotid & Lacrimal glands by ↑ uptake by mediastinal LN



"PANDA SIGN"



"LAMBA SIGN"

Rx Steroid + Immunosuppression.

↑ LEVELS OF ACE

- 1> Sarcoidosis
- 2> Leprosy
- 3> Gaucher's Disease
- 4> Hyperthyroidism
- 5> Disseminated granulomatous infec' such as.
6> miliary TB

Pneumonia [Sar Le Ga DM ~~Hyper~~ thymo wale]

CONNECTIVE TISSUE DISORDER + LUNG

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RA

- M/c pulmonary manifestation
→ pleuritis
- Low Glucose Pleural Effusion
- ILD → NSIP, B'xis
- Rheumatoid ~~Asthma~~ nodule
- CAPLAN's syndrome: RA +
[Pneumoconiosis]
[silica expo, coal expo]

SLE

- M/c pul. manifestation = Pleuritis
- Acute Lupus pneumonitis.
⇒ Pulmonary capillaritis +
diffuse alveolar H'ge
- ILD → NSIP.
- Shrinking Lung syndrome



Diaphragmatic involvement in SLE.

SCLERODERMA

HIDE BOUND CHEST.

ILD NSIP → UIP, Pul. HTN

Mrc of death in scleroderma → Pulmonary cause

POLYMYOSITIS

- ↑ Anti JO1 ABS (
- Anti Synthetase Sx.
- C/F - 1) Fever
2) Myositis
3) ILD
4) Arthritis
5) Mechanic Hand

DIFFUSE ALVEOLAR HYG / Pul HEMOSIDEROSIS

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IDIOPATHIC Pul. hemosiderosis

- 1) Intra alveolar bleed
- 2) Fe accumulation as hemosiderin in alveolar macrophages
- 3) Fe deficiency anaemia

Pul. RENAL SYNDROME

- 1) SLE.
- 2) Good Pasture Syndrome
- 3) Small vessel vasculitis
 - ↳ Wegener's granulomatosis
 - 1) Necrotising granulomatous vasculitis
 - URT → epistaxis, sinusitis
 - LRT → cavities, Diff-Alv-Hyg
 - 2) RPGN
 - 3) necrotising involvement of URT → epistaxis, sinusitis
LRT → cavities, Diff-Alv-Hyg

OCCUPATIONAL

LUNG DISEASES

SILICOSIS

H/C occupational lung disease worldwide

$< 2.5 \mu$ = Dangerous particles

ASBESTOSIS

occupation ship building, construction workers

Particle ~~~ curly serpentene
~~~~ straight amphibole  
(carcinogenic)

### FEATURES



1) Pleural Plaques

↳ Most specific for asbestos

2) Fibrosis

- of duration & exposure

### SILICOSIS

sand blasting, quarrying

crystalline silica  
Amorphous silica  
1) silicotic nodules



2) Merging of nodules → coal macules  
progressive massive fibrosis

### COAL-WORKERS PNEUMOCONIOSIS

Coal miners

Anthracite Bituminous

1) ~~Anthracosis~~

1) Anthracite

2) Bituminous

1) Anthracosis

2) Merging of nodules → coal macules

progressive massive fibrosis

3) complicated CWP

4) ↑ COPD

3) Benign pleural effusion.

4) M/c malignancy associated w/ it  
↓

LUNG CANCER

Smoking + asbestos.  
⇒ synergistic

Most specific  
↳ MESOTHELIOMA

Lower zone Disease

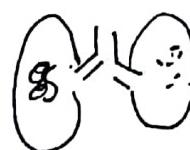
3) Silico-TB:- Chronic exposure

4) Alveolar proteinosis  
Acute exposure

5) Malignancy.  
CXR - Hilar LN +  
egg shell calcification

5) Malignancy

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### Round Atelectases



Organised Plegg. around segment

↓  
Localised atelectasis

↓  
COMET TAIL appearance

Upper zone Disease

### SLEEP APNOEA

Apnoea - cessation of airflow for at least 10 sec.

Hypopnoea - > 30% reduction in airflow associated w/  
> 3% fall in  $\text{SpO}_2$ .

## SLEEP APNOEA

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CENTRAL

Resp. effort (-)

Afnoee +

Ruf. drive Θ

## OBSTRUCTIVE

Apnoea 6

## Persisting Res. effect

↑ Collapsibility of airway  
at Neck.

e.g. CHF

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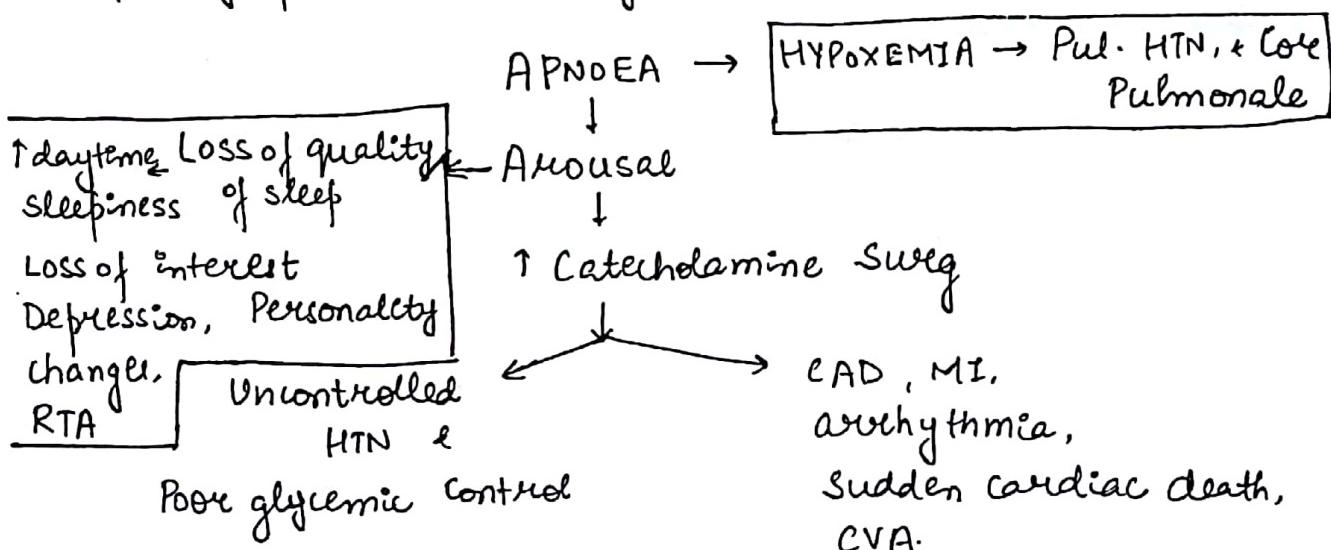
## Narcotic Abuse

## R/F for obstructive Sleep Apnoea :-

- 1) Obesity
  - 2) O<sup>↑</sup>
  - 3) Craniofacial Ab (1)
  - 4) Hypothyroidism
  - 5) Adenohypophyseal

## PATHOPHYSIOLOGY-

H/c Symptom → Snoring.



## Gold Std A :- Polysomnography

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- |                     |                                  |
|---------------------|----------------------------------|
| 1> EEG.             | 6> Oronasal flow                 |
| 2> EOG              | 7> Snore mic                     |
| 3> ECG              | 8> Thorax + Abd. movement sensor |
| 4> EMG              | 9> Body position / Limb movement |
| 5> SpO <sub>2</sub> |                                  |

Other scales for assessment :-

- 1> Epworth Sleepiness Scale
- 2> STOP BANG Questionnaire.

SEVERITY of OSA  $\Rightarrow$  APNOEA HYPOPNEA INDEX (AMI)

No. of Apnoea + Hypopnoea  
Hour.

< 5/hr  $\Rightarrow$  N

5-14/hr  $\Rightarrow$  Mild OSA  $\rightarrow$  Behavioural Rx

15-29/hr  $\Rightarrow$  Mod. OSA  $\left.\right\} \text{Medical Rx of choice}$

$\geq 30/\text{hr} \Rightarrow$  Severe OSA CPAP - mild OSA +  
comorbidities

In few cases  $\rightarrow$  Uvulo palatopharyngoplasty.

# MALIGNANCY

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## 1° LUNG MALIGNANCY :-

Non-Small Cell Lung Cancer (NSCLC)

Small cell Lung cancer (SCLCC)

- 1) Adeno Ca Mc worldwide
- 2) Sq. cell Carcinoma Mc in India
- 3) Large cell "

- 1) Small cell ca / oat cell tumour.

## LOCATION & ASSOCIATION OF TUMOURS :-

1) Central Location  
Cigarette smoking

⇒ Sq. cell  
small cell (strongest association)  
Endobronchial Location.

2) Peripheral Location  
Less smoking

⇒ Adeno ca (♀, young ♂, less smoker)  
Large cell

3) Cavitation

Squamous  
Large.

|                                 | ADENO                                                                                                           | SQUAMOUS                                                                                                       | SMALL CELL                                                                                                                                             |
|---------------------------------|-----------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|
| Oncogene                        | KRAS / EGFR / ALK                                                                                               | FGFR, PI3K                                                                                                     | my c, BCL2B5                                                                                                                                           |
| Biopsy                          | Glandular differentiation                                                                                       | Keratinisation + intercellular keratin bridges                                                                 | Small round cell = hyperchromatic nuclei                                                                                                               |
| Features                        | → Lepidic pattern<br>Lung → Lung metastasis<br>Scar Ca → Adeno ca<br>↑ Clubbing → Hypertrophic osteoarthropathy | Central Cigarette Cavity<br>Calcinosis ↑ parathyroid Life threatening<br>↑ parathyroid hormone related peptide | ② chemo + radio sensitive<br>Rapid recurrence<br>↑ metastasis<br>↑ SVC obstruction<br>POOR PROGNOSIS<br>clubbing is rare<br>↑ Paraneoplastic Syndromes |
| Paraneoplastic<br>↳ Hematologic |                                                                                                                 |                                                                                                                |                                                                                                                                                        |

### PARANEOPLASTIC associated in SCLC

- 1) Hyponatremia - SIADH
  - 2) Hypokalemia - ectopic ACTH
  - 3) Hypocalcemia - Calcitonin
  - 4) Lambert Eaton Syndrome
- Mice of ectopic ACTH ↓  
SCLC.

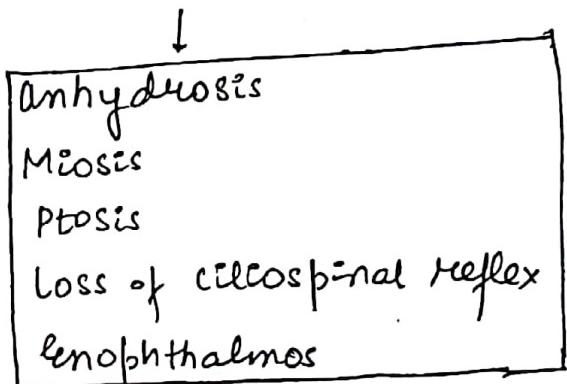
### CLINICAL MANIFESTATIONS of SCLC

- 1> Irritation → Cough (M/e symptom)
- 2> Hemoptysis - tumour infiltrates vessel
- 3> ↑ size & cause → Bronchial obstruction (Fever, SOB)
- 4> Pleural involvement → Pleuritis  
Chest pain, Pleural eff. → SOB.



- 5) Skin & Intercostal n/vs. → chest pain.
  - 6) Pericarditis / Pericardial effusion.
  - 7) Esophagus → dysphagia
  - 8) Recurrent Laryngeal n/r → Hoarseness of voice
  - 9) SVC obstruction.
  - 10) Stellate Ganglion → HORNER's Syndrome  
(sympathetic ganglion)

Migratory thrombophlebitis  
= Trousseau's Syndrome  
+ clubbing = Adeno Ca



- ii) Distant Metastasis      :- Brain / Bone / Liver.  
 H/c site → Brain  
 Most specific → Adrenals.

## INVESTIGATIONS 2

- ⇒ CYTOLOGY      → sputum      } malignant cells  
                        → pleural fluid }

- 27 CXR - PA - Solitary Pnlm. nodule  
Collapse.  
LN ↑  
Pleural eff

- 37 CT- Chest - Precise anatomical Location.

- 4) Gold Std → BIOPSY < CT guided  
Bronchoscopy

5> PET SCAN - staging

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6> Bone Scan

Rx

NSCLC

Resectable

Stage I, II, IIIA

Surgery

Unresectable

III B, IV

Medical Rx

Squamous

Cisplatin

+ Gemcitabine/ Paclitaxel

SCLC

Medical Rx

Chemo Rx + Radio Rx.

Cisplatin + Etoposide

Adeno

Cisplatin +  
Pembrolizumab.

Targeted Rx

EGFR Antagonist -  
Erlotinib, gefitinib

ALK Antagonist

Crizotinib.

Adeno ♂ / non-smoker / Asian  $\Rightarrow$  EGFR mutation.

Pancoast Tx - usually occurs in Sq cell

Located at apex.

May involve stellate ganglion.

PANCOAST SYNDROME = 1> Tumour in Lung Apex

2> Involve  $\rightarrow$  1st 2 ribs

$\rightarrow$  Stellate Ganglion.

$\rightarrow$  C8 T1 T2  $\rightarrow$  Pain & weakness in ulnar distribution

## TUBERCULOSIS

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## Tables      NOMENCLATURE

## Tabes Pulmonale - Pul-TB (H/c)

## Tubes mesentrica - Abd. TB

Carries SICCA - Shoulder TB

## Pott's Disease - Spinal TB

*Spina ventosa* - TB Dactylella.

Scrofula - LN TB (M/c extrapulmonary)

*Lupus vulgaris* - Skin TB

## Poncet Disease - TB Rheumatism

ORGANISM & LAB DIAGNOSIS

1) Direct Microscopy → ZN staining / Led FM

Under ZN staining to visualize each mL of sputum should contain 10,000 bacilli

27 Solid Culture → LJ media 6-8 weeks

3) Liquid      => BACTEC  
                  MGIT  
                  Sept. check }  
                  6-8 weeks +ve result  
                  7-10 day

## 47 Rapid Molecular Method

a) CBNAAT → / Gene expert → TB Bacilli + Ref. sensitivity  
2 hours.

by Line probe assay | LPA → TB Bacilli + Drug  
Sensitivity (1st Line + 2nd Line drug) = 48-72 hours

Most Rapid method to identify of TB → Direct microscopy  
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Most Rapid method for Rifampicin sensitivity = Gene expert

### PRESUMPTIVE TB

Any one of the following

Cough > 2 wks

Fever > 2 weeks

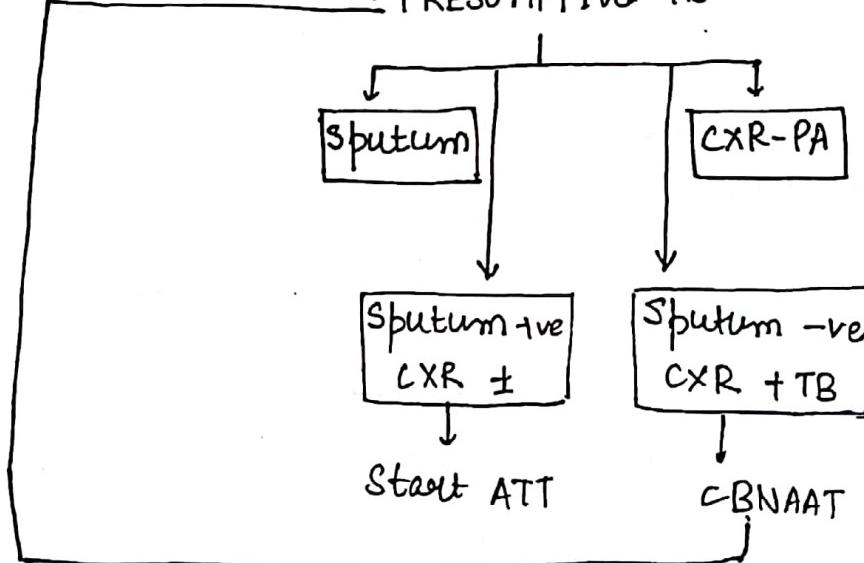
Hemoptysis

wt. loss

Abnormalities on CXR - PA view

### ALGORITHM FOR A of TB

Pt / HIV → PRESUMPTIVE TB



### IGRA / Quantiferon Gold

Advantages:-

- 1> TB specific Ag → CFP & ESAT used
- 2> Less cross-reactivity = BCG, Non-Tubercular mycobacterium
- 3> Blood Test
- 4> Serial Testing can be done to out boosting phenomena
- 5> Single visit to hospital.

## Disadvantage

Can't differentiate Infection vs Active disease

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## PATHOLOGY

1° TB → unsensitised individual

2° TB / Post 1° TB → sensitised individual

Reinfection  
Reactivation

### 1° TB

→ TB bacilli → mid + lower zone

→ Area of 1st contact

1° focus / Ghon's focus

→ Alveolar macrophage engulf TB bacilli



① Phagolysosome fusion



↑ survival of M.tb.

→ For immunity macrophages reach hilar LN ⇒ LN ↑

Ghon's complex → Ghon's focus + LN ↑

In LN ->

↑ TH<sub>1</sub> response

\* ↑ IFN-γ, TNFα



↑ killing capacity of macrophage



Limit TB

Memory cells are formed



## **2° TB**



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- TB bacilli reach apex & actively grow.
- Bodys immune response will try to wall off infection.
- After few weeks, Delayed Type HSN Response FB produced & destroys TB bacilli & Lung Parenchyma
- 2° TB is more infectious & it is active disease.
- Calcified Ghon's Complex ⇒ Reinke's Complex.

## TB/HIV

- \* If ART is started 1st → ↑ Risk of immune reconstitution inflammatory syndrome (IRIS)
- Start ATT 1st & merge ART in 2 weeks. to 2 months

ATT = Always The Treatment

- \* If pt. is on TLE regimen. → Rifampicin can be given
- If pt. is on Neviparine / Protease Inhibitor
  - ↓
  - Rifampicin can't be given
  - Rifabutin is given.

DISSET

## DISSEMINATED TB

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### CLASSICAL MILITARY TB

1<sup>o</sup>/2<sup>o</sup> form

Hematogenous / Lymphogenous spread.

Pathognomonic  $\rightarrow$  Chonoidal Tubercles

Sputum  $\rightarrow$  -ve

CXR - 1-2mm, Blz symmetric

Homogeneous, millet shaped shadowing

### CRYPTIC MILITARY TB

Elderly, chro. symptom

Fever, wt. loss, anaemia

CXR - N

Sputum  $\rightarrow$  -ve

Pt. collapses  $\Rightarrow$  death  $\rightarrow$  autopsy reveals meningeal tubercles

This is also military TB. but hidden one CXR.

## NON-REACTIVE (or) AREACTIVE TB

Rare form

Acute Septicaemic form.

Underlying hematological abnormality

Fatal form

Autopsy shows areas of necrosis  $\pm$  granuloma formation

Rx

New Case = 2HRZE + 4HRE = 6 months = DAILY

Previously Rx = 2HRZES + 1HRZE + 5HRE = 8 months = DAILY

HDRTB = Resistance to both H & R = DAILY

6-9 mnths  $\rightarrow$  E + Z + Kanamycin + Levoflox + Cycloserine + Ethionamide

18 mnths  $\rightarrow$  E + Levoflox + Cycloserine + Ethionamide

XDR-TB :- MDR-TB + Resistance to 1<sup>st</sup> line aminoglycoside  
+ Resistance to 1 FQ

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6-12 month = capreomycin + Moxi + PAS + Clofazamine +  
High dose INH + Amoxyclav + Linezolid

18 months = Moxi + PAS + Clofazamine + High Dose INH +  
Amoxyclav + Linezolid

(24 - 30 months)

### NEWER Anti - TB Drugs

BEDAQUILINE / Sartura

2012

Diaxyl quinolone

MOA:- ATP synthase inhibition

S/E - QT Prolongation

DR TB.

Conditional access in India

DELAMANID

2014

Nitroimidazole

MOA:- Mycolic acid synthase inhibitor

S/E - QT Prolongation

DR TB

Soon available in India

Dose - 400mg

duration - 24 weeks.

A

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# ACIB, BASE, BALANCE & ABG

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## I) NORMAL VALUES

pH 7.35 - 7.45      pH  $\leq$  7.35  $\Rightarrow$  Acidosis

P<sub>a</sub>CO<sub>2</sub> 35-40 mmHg      pH  $\geq$  7.45  $\Rightarrow$  Alkalosis

HCO<sub>3</sub><sup>-</sup> 22-26 meq      (N) P<sub>a</sub>CO<sub>2</sub> = 40

P<sub>a</sub>O<sub>2</sub> 70-100 mmHg      HCO<sub>3</sub><sup>-</sup> = 26.

## II) Relation Between pH, P<sub>a</sub>CO<sub>2</sub> & HCO<sub>3</sub><sup>-</sup>

↳ Henderson Hasselbach equation

$$\text{pH} = 6.1 + \log \frac{[\text{HCO}_3^-]}{\text{P}_{\text{aCO}_2} \times 0.03} \Rightarrow \text{pH} \propto \frac{\text{HCO}_3^-}{\text{P}_{\text{aCO}_2}}$$

$$\downarrow \text{pH} \uparrow \propto \frac{\text{HCO}_3^- \uparrow}{\text{P}_{\text{aCO}_2} \uparrow} \Rightarrow \frac{\text{BASE}}{\text{ACID}}$$

## III) REGULATION OF PH P<sub>a</sub>CO<sub>2</sub> & HCO<sub>3</sub><sup>-</sup>

Lungs  $\uparrow \downarrow \text{CO}_2 \Rightarrow$  Resp. process

Kidneys  $\uparrow \downarrow \text{HCO}_3^- \Rightarrow$  Met. process

## SIMPLE ACID BASE DISORDER

1° process + Adequate compensatory response

Respiratory Acidosis

pH  $\downarrow$  P<sub>a</sub>CO<sub>2</sub>  $\uparrow$  HCO<sub>3</sub><sup>-</sup>  $\uparrow$

Metabolic Acidosis

pH  $\downarrow$  P<sub>a</sub>CO<sub>2</sub>  $\downarrow$  HCO<sub>3</sub><sup>-</sup>  $\downarrow$

Resp. Alkalosis

pH  $\uparrow$  P<sub>a</sub>CO<sub>2</sub>  $\downarrow$  HCO<sub>3</sub><sup>-</sup>  $\downarrow$

Metabolic alkalosis

pH  $\uparrow$  P<sub>a</sub>CO<sub>2</sub>  $\uparrow$  HCO<sub>3</sub><sup>-</sup>  $\uparrow$

In simple acid base disorder, always  $1^{\circ}$  change & compensation move together 236

In  $1^{\circ}$  resp. process  $\rightarrow$  change in pH w.r.t.  $\text{PaCO}_2 + \text{HCO}_3^-$  in opposite direc'

In  $1^{\circ}$  met. process - change in pH w.r.t.  $\text{PaCO}_3 + \text{HCO}_3^-$  in same direction

### ROME

resp. opp., met. same direction.

Q. pH = 7.33,  $\text{PaCO}_2 = 60$ ,  $\text{HCO}_3^- = 34$   
↓              ↑              ↓ :  $\Rightarrow$  Resp. Acidosis  
acidosis

Q. pH = 7.48,  $\text{PaCO}_2 = 26$ ,  $\text{HCO}_3^- = 16$   
↑              ↓              ↓ :  $\Rightarrow$  Resp. Alkalosis  
alkalosis

Q. pH = 7.27,  $\text{PaCO}_2 = 25$ ,  $\text{HCO}_3^- = 10$   
↑ ↓              ↓              ↓ :  $\Rightarrow$  Met. Acidosis

Q. pH = 7.55,  $\text{PaCO}_2 = 50$ ,  $\text{HCO}_3^- = 40$   
↑              ↑              ↑ :  $\Rightarrow$  Met. Alkalosis

## COMPENSATION

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### Resp. Acidosis

Acute For every 10mmHg ↑  $\text{PaCO}_2$ ,  $\text{HCO}_3^-$  ↑ by 1 meq.

Chronic For every 10mmHg ↑  $\text{PaCO}_2$ ,  $\text{HCO}_3^-$  ↑ by 4 meq

### Resp. Alkalosis

Acute For every 10mmHg ↓  $\text{PaCO}_2$ ,  $\text{HCO}_3^-$  ↓ by 2 meq

Chronic " " 10mmHg ↓  $\text{PaCO}_2$ ,  $\text{HCO}_3^-$  ↓ by 4 meq

Q Acute F.B. ingestion, pH = 7.32,  $\text{PaCO}_2$  = 70,  $\text{HCO}_3^-$  = 29.

↓                    ↓                    ↑                    ↑  
 Acidosis.

$$40 \xrightarrow{30} 70 \quad 26 \xrightarrow{3} 29.$$

Resp. acidosis is compensated by met. alkalosis.

Q Chr. neuromuscular disorder

$$\begin{array}{ccc} \text{pH} = 7.34 & \text{PaCO}_2 = 60 & \text{HCO}_3^- = 34 \\ \downarrow & \uparrow & \uparrow \end{array}$$

Chr. resp. acidosis

$$40 \xrightarrow{20} 60 \quad 26 \xrightarrow{8} 34$$

Ans:- Chr. resp. acidosis is compensated by met. alkalosis.

Chr. compensated Resp. Acidosis.

## Metabolic Acidosis

$$\text{Acute expected } \text{PaCO}_2 = (1.5 \times \text{HCO}_3^-) + 8 \pm 2. \quad [\text{winter's formula}]^{238}$$

Q. pH = 7.27,  $\text{HCO}_3^- = 10$ ;  $\text{PaCO}_2 = ?$

$$(1.5 \times 10) + 8 \pm 2$$

$$15 + 8 \pm 2$$

$21 - 25 \Rightarrow \text{compensated}$

Q. pH = 7.26,  $\text{PaCO}_2 = 18$ .  $\text{HCO}_3^- = ?$

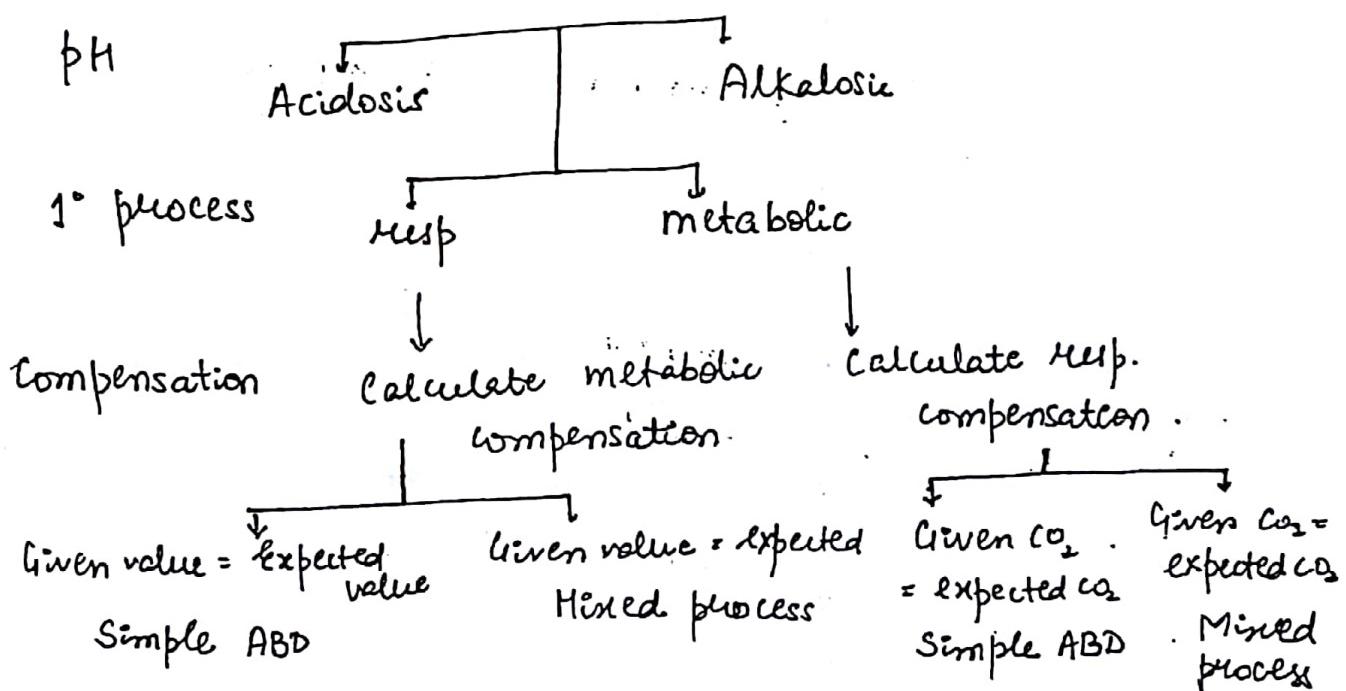
$$(1.5 \times 6) + 8 \pm 2 = \cancel{9} \pm 2. \quad \cancel{9} \pm 2 = 7 \pm 1.$$

$$9 + 8 \pm 2 = 17 \pm 2 = 15 - 19$$

Met. acidosis  $\approx$  compensatory alkalosis

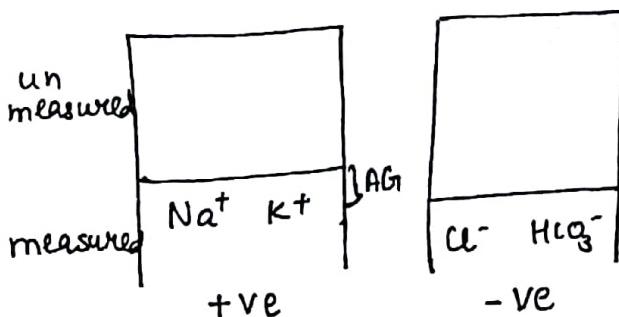
## Metabolic Alkalosis

$$\text{Expected } \text{PaCO}_2 = [\text{HCO}_3^- + 15]$$



## METABOLIC ACIDOSIS & CONCEPT OF ANION GAP

239



$$(Na^+ + K^+) - (Cl^- + HCO_3^-) = \text{Anion Gap.}$$

$$(Na^+ + K^+) + \text{unmeasured} = (Cl^- + HCO_3^-) + \text{Cations} \quad \text{unmeasured anions}$$

$$(Na^+ + K^+) - (Cl^- + HCO_3^-) = \text{unmeasured anions} - \text{unmeasured cations}$$

$$[\text{Anion Gap}] = \text{unmeasured anions} - \text{unmeasured cations}$$

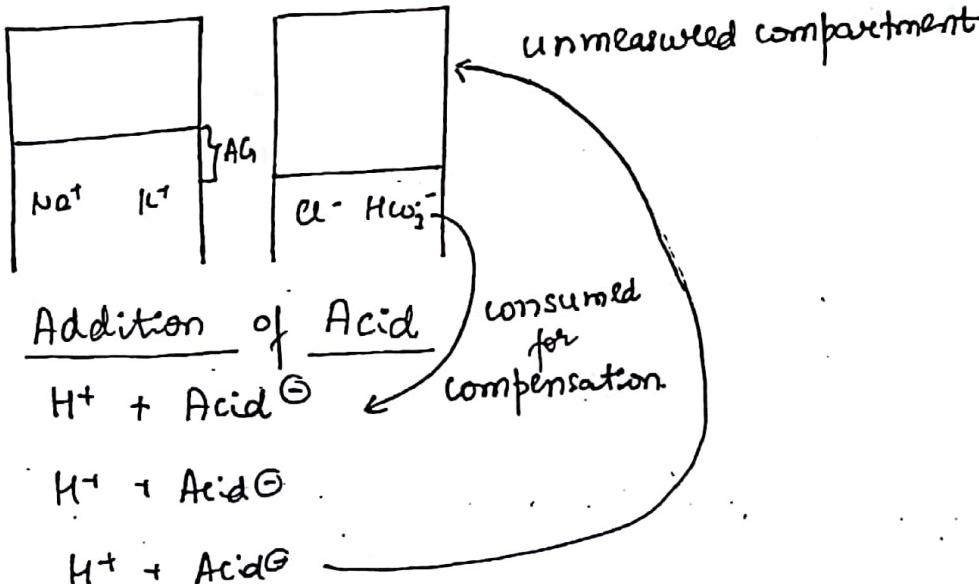
Common cause of ↑ in Anion Gap = ↑ in unmeasured anions

New formula for Anion Gap

$$(Na^+) - (Cl^- + HCO_3^-) = AG$$

8-12 mEq.

## HIGH AG METABOLIC ACIDOSIS



In pure High AG Metabolic Acidosis

240

Rise in AG = fall in  $\text{HCO}_3^-$

$\text{AG} - 10 = 25 - \text{Given carbonate}$ .

$$\Delta \text{AG} = \Delta \text{HCO}_3^-$$

### CAUSES :-

- I) TOXINS / DRUGS -
  - 1) Methanol
  - 2) Paraldehyde
  - 3) Ethylene glycol / antifreeze
    - ↳ oxalic acid.
    - oxaluria
  - 4) Salicylates
- II) Ketoacidosis -
  - 1) DKA
  - 2) Alcoholic ketoacidosis
  - 3) Starvation
- III) Renal Failure

### IV) Lactic Acidosis

a) Type A Lactic Acidosis  $\Rightarrow$  [Hypoxemia  
 $\downarrow$  perfusion]

e.g. shock

Anaemia

CO poisoning

b) Type B Lactic Acidosis = [Perfusion: N]

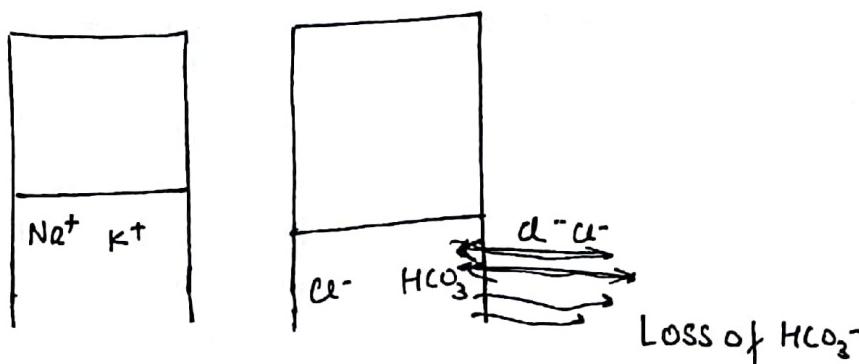
e.g. Renal failure

Hepatic failure

Drugs - metformin  
zidovudine

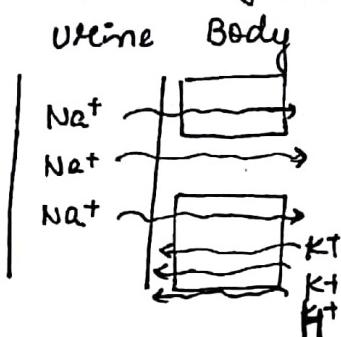
## (N) AGI METABOLIC ACIDOSIS

241

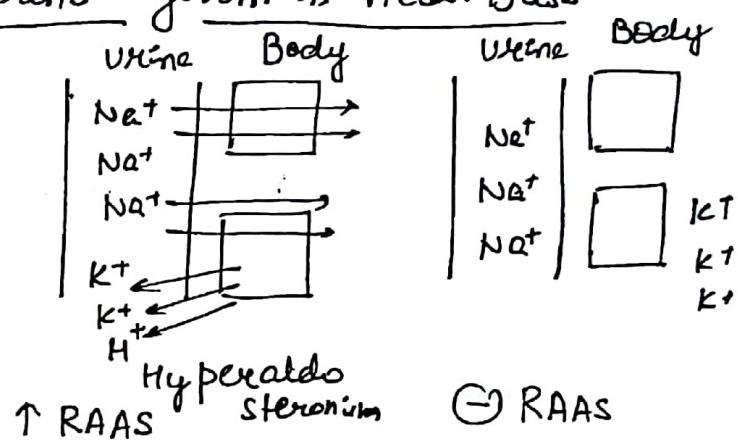


Hyperchloremic Metabolic Acidosis

### RENIN - Angiotensin - Aldosterone System in Acid. Base



(N)



Hypokalemia  
+  
Met. alkalosis

Hypoadosteronism  
Hyperkalemia +  
Met. acidosis

### CAUSES

#### I) GIT CAUSE

- 1) Diarrhea
- 2) Pancreatic fistula
- 3) Uretero sigmoidostomy
- 4) Enterocutaneous fistula

#### II) RENAL CAUSE

- 1) RTA
- 2) Drugs
  - ① Carbonic anhydrase inhibitor
  - ② ACEI
  - ③ ARB
  - ④ Aldosterone antagonist

# RTA

## Type I RTA

## Type II RTA

Met. acidosis + hypokalemia

242

## Type IV RTA

met. acidosis +  
Hyperkalemia  
(H/c type)

### causes

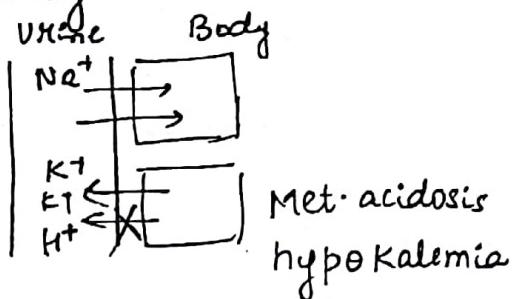
Hyporenemic state  
Aldosterone resistance  
" deficiency

Hyporenemic state  
↳ Diabetic nephropathy  
↳ Chro. tubulo interstitial

## Type I RTA

### - Distal RTA

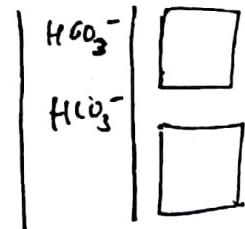
- $\text{H}^+$  excretion lost at collecting Duct.



## Type II RTA

### Proximal RTA

$\text{HCO}_3^-$  reabsorption lost in PCT

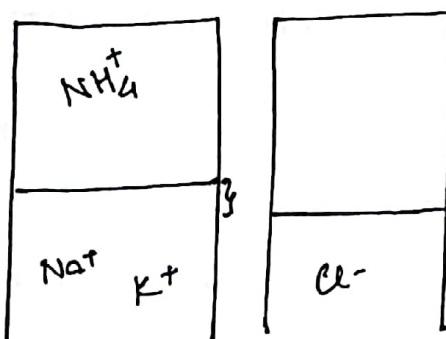


Bicarbonaturia can  
induce Kaliuresis  
Met. acidosis +  
Hypokalemia

## Urine anion gap :-

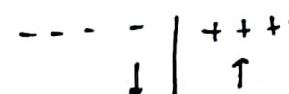
To differentiate N anion gap Met acidosis of diarrhoea <sup>243</sup> v/s

RTA



$$UAG = [Na^+ + K^+] - Cl^-$$

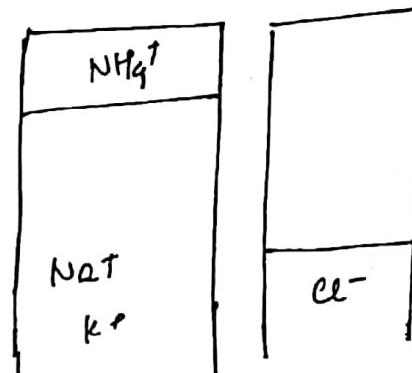
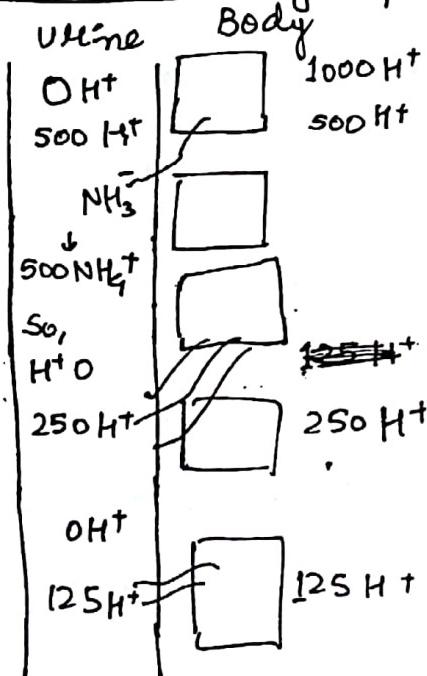
N value = 0-5.



taking 0 as reference level

(N)

## Renal Handling of Acid

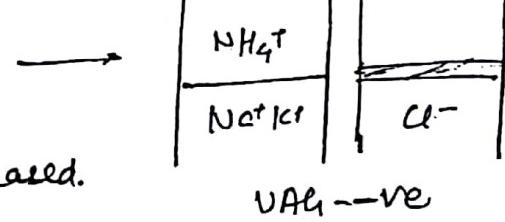


$$RTA = UAG + ve.$$

Diarrhoea :- Met. acidosis.

10,000 H+

Urinary NH4+ is increased.



RTA -

UAG is indirect measure of urinary NH4+ excretion.

UAG is negative in GIT cause diarrhoea  
GIT

## METABOLIC      ALKALOSIS

244

Initiating event

Persisting event

- 1) ECFV contract<sup>n</sup>, hypotension.
- 2) ↓ 1° mineralocorticoid excess → ECFV expand<sup>n</sup> & HTN  
(B) initiating + persisting event)

SALINE    RESPONSIVE / Cl<sup>-</sup> response  
UCl<sup>-</sup> < 20 mEq

- 1) vomiting
- 2) Ryle's Tube aspiration
- 3) Diuretic use
- 4) Post hypercapnic Met. alkalosis

SALINE    UNRESPONSIVE / Cl<sup>-</sup> unresponsive  
UCl<sup>-</sup> > 20 mEq

- 1) 1° Hyperaldosteronism
  - 2) Cushing's syndrome
  - 3) Renin secreting Tumour
  - 4) Renal artery stenosis
  - 5) Liddle's Syndrome
  - 6) Bartter Syndrome
  - 7) Gitelman Syndrome
- HTN      hypo tension

## RESPIRATORY      ACIDOSIS

Type 2 Resp. Failure

## RESPIRATORY      ALKALOSIS

CHRONIC Resp. Alkalosis :-

M/c acid base Ab(N) in critically ill pt

- 1) Pain, Panic, Psychogenic, Progesterone  
⇒ Hyperventilation
- 2) Aspirin
  - a) vomiting → met. ~~acidosis~~ alkalosis

2) High AG metabolic acidosis.

→ When aspirin goes to blood



Metab. alkalosis.

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3) Theophylline

4) Fever, sepsis (change in sensitivity of Resp. centre)

5) CHF → Pul. oedema → stimulate of chemoreceptors

6) Cirrhosis of Liver → ↑ Glutamate

7) Severe Hypotension Hypoxemia → hyperventilation

8) ↑ ICP

ICU pts are also prone to Resp. alkalosis due to  
pain, panic, psychogenic

Q. pH = 7.32,  $\text{PaCO}_2 = 60$ ,  $\text{HCO}_3^- : 34$ . ↓ ↑ ↑ = <sup>che. compensated</sup>  
<sup>Given value > Expected</sup>  
 $90 \xrightarrow{20} 60$        $26 \xrightarrow{8} 34$  <sup>HCO\_3^-</sup>  
Resp. Acidosis

Q. pH 7.35,  $\text{PaCO}_2 = 60$ ,  $\text{HCO}_3^- = 40$ . ↓ ↑ ↑ = Given value > Expected  
Metab. Resp. acidosis + Add. metabolic alkalosis

Q. pH 7.28  $\text{PaCO}_2 = 60$ ,  $\text{HCO}_3^- = 26$ . ↓ ↑ ↑ = Given value < Expected  
Metab. Resp. acidosis + Add. metabolic acidosis

AG High AG or Normal AG.

246

In pure High AGMA  $\Delta AG = \Delta HCO_3^-$

Rise in AG = fall in  $HCO_3^-$

$$[\text{Given AG} - 10] = [25 - \text{Given } HCO_3^-]$$

Q. Pt. is having DKA.

$$\text{pts AG} = 20 \quad HCO_3^- = 15$$

$$\Delta AG = 20 - 10 \quad \Delta HCO_3^- = 25 - 15 \\ 10 \qquad \qquad \qquad 10$$

$\Rightarrow$  Pure AG Met. Acidosis.

Q. Pt is DKA.

$$\text{Pt. AG} = 20 \quad HCO_3^- = 20$$

$$\Delta AG = 10 \quad \Delta HCO_3^- = 25 - 20 = 5$$

$\Delta AG > \Delta HCO_3^- \rightarrow$  Additional metabolic acidosis: alkalosis

<sup>High</sup>  
Additional AGMA + addition Met. Alk

Q. DKA  $AG = 20 \quad HCO_3^- = 10$

$$\Delta AG = 20 - 10 \quad \Delta HCO_3^- = 25 - 10 \\ = 10 \qquad \qquad \qquad = 15$$

$$\Delta AG < \Delta HCO_3^-$$

High AGMA +  $\textcircled{N}$  AG metabolic acidosis

Compare  $\Delta AG$  &  $\Delta HCO_3^-$  relation.

247

$\Delta AG = \Delta HCO_3^- \Rightarrow$  Pure AGMA

If  $\Delta AG > \Delta HCO_3^- \Rightarrow$  AGMA + additional met.  
alkalosis

If  $\Delta AG < \Delta HCO_3^- \Rightarrow$  AGMA + additional met.  
acidosis

Q      pH - 7.2       $P_{CO_2} - 60$        $HCO_3^- - 19$   
      ↓                  ↑                  ↓

~~Acidosis~~ Acidosis (mixed disturbance)

Reported.

20.



# NEPHROLOGY

# PHYSIOLOGY

250

Kidney performs Diverse func' :-

- 1> Excretory :- urine formation
- 2> Homeostasis :- water & acid base balance
- 3> Hormonal :- erythropoietin synthesis & Vit D activation.

## RENAL BLOOD FLOW

Kidneys are highly vascular.

Receives 25% of c. output

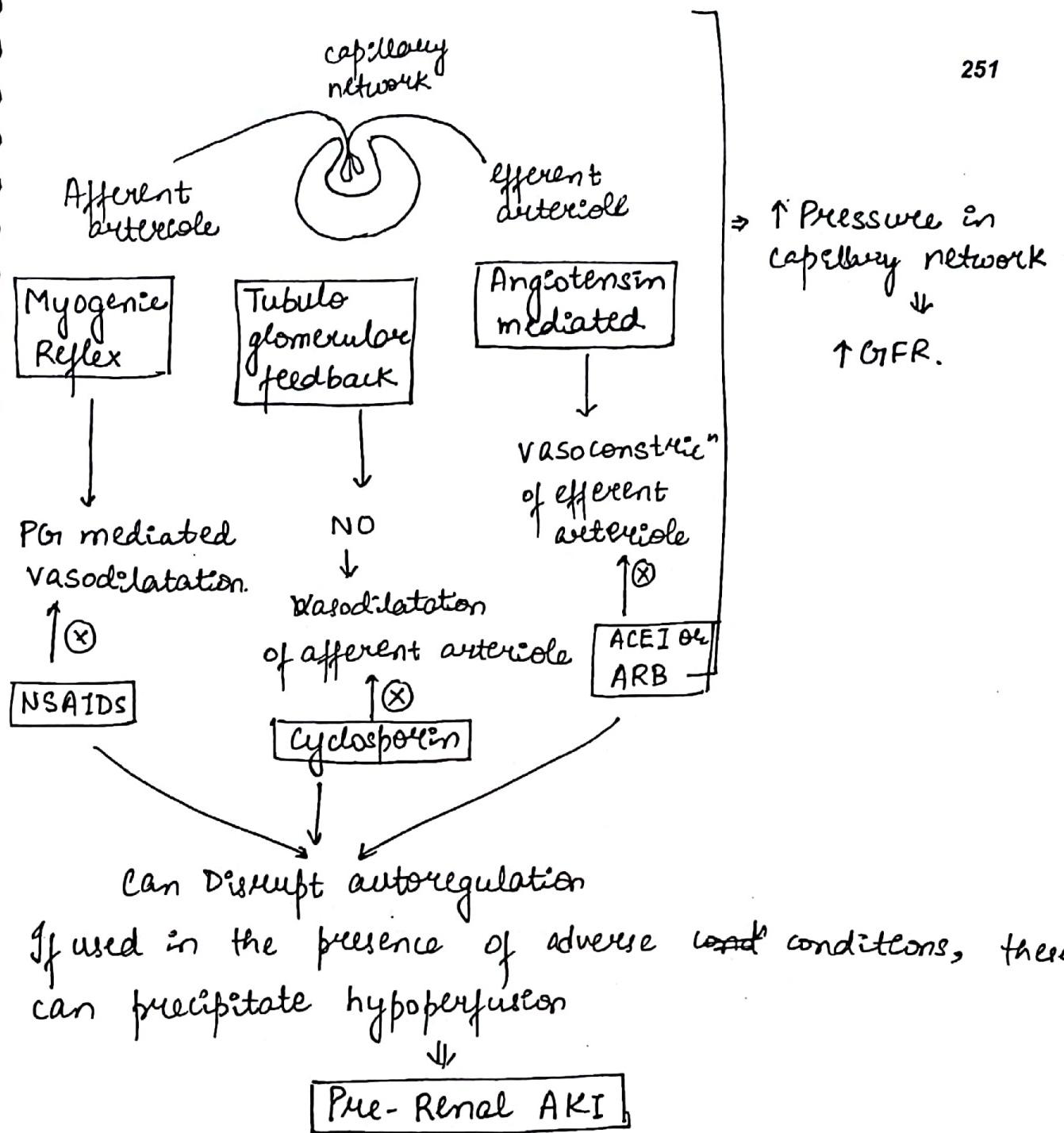
Even in presence of adverse cond' to the renal blood flow -

- 1> Dehydration
- 2> Hypotension
- 3) Renal artery stenosis

↓  
Autoregulatory mechanisms activated

↓  
Maintain adequate GFR.

- 1) ↑ Glomerular capillary Pressure



## RENAL ARTERY STENOSIS

Cause → 1) 90% → atherosclerosis/arteriosclerosis

2) 10% → FMD (fibromuscular Dystrophy)

Pathophysiology →

Activates RAAS

Vasoconstriction

 $\text{Na}^+/\text{H}_2\text{O}$  retenison.M/I/C C/F  $\rightarrow$  Sy. HTN

[M/I/C cause - 2° HTN - Renovascular]

**ESG GUIDELINES** - evaluation + Management

When to suspect/ screen for R.A.S.?

- 1) young HTN (onset <30 yrs of age)
- 2) severe HTN <55 yrs of age ( $>160/110 \text{ mm of Hg}$ )
- 3) HTN emergencies (sudden  $\uparrow$  BP  $\pm$  target organ damage)
- 4) Refractory HTN (uncontrolled  $\geq 3$ , 1st is a diuretic)
- 5) Decline in GFR  $>30\%$  after ACEI therapy (Disrupts autoregulation)
- 6) Asymmetrical kidneys on USG ( $D_{\text{diff.}} \geq 1.5 \text{ cm.}$ )
- 7) Unexplained Renal failure

| Screening Tests                                                                         | Specific                                                                                |
|-----------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <u>Duplex Doppler</u> (Best)<br>- >98% sensitivity<br>- Non-invasive, easy available | 1) Conventional Renal angiography<br><u>GRADING</u><br>% of stenosis      Severity + Rx |
| 2) <u>CT-Renal Angiography</u><br>4/I $\rightarrow$ GFR $\leq 60 \text{ mL/min}$        | <50% (Mild)      No further testing                                                     |
| 3) <u>MR-Renal angiography</u><br>4/I $\rightarrow$ GFR $\leq 30 \text{ mL/min}$        | 50-70% (Moderate)      Follow-up                                                        |
| 4) <u>DTPA Scan</u> (radio-isotope)<br>(functional assessment of kidney)                | >70% (severe)      Always haemodynamically significant<br>↓<br>Elective Rx              |

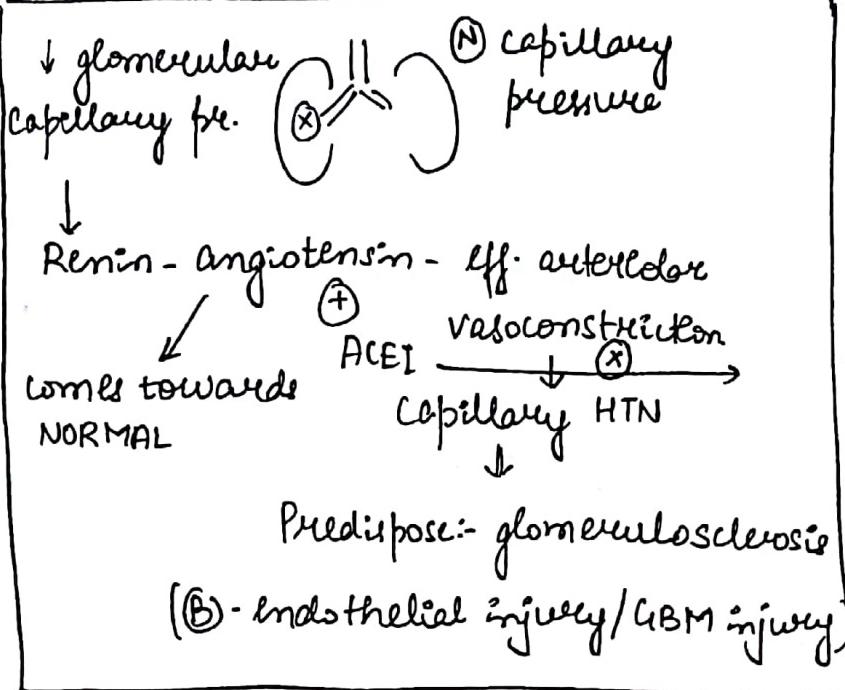
Rx 1st line → Medical

|                                    |                  |
|------------------------------------|------------------|
| U/L                                | B/L              |
| ACEI                               | ACEI - C/I       |
| (only drug c<br>protects N Kidney) | CCB<br>β blocker |
|                                    | Diuretic         |

MOA of ACEI in U/L RAS.

## Angioplasty 253

- 1) All - severe RAS
- 2) cause in FMD  
(focal stenosis → so, easily Rx  
c angioplasty)
- 3) Refractory Heart failure  
(Flash Pulmonary Oedema)

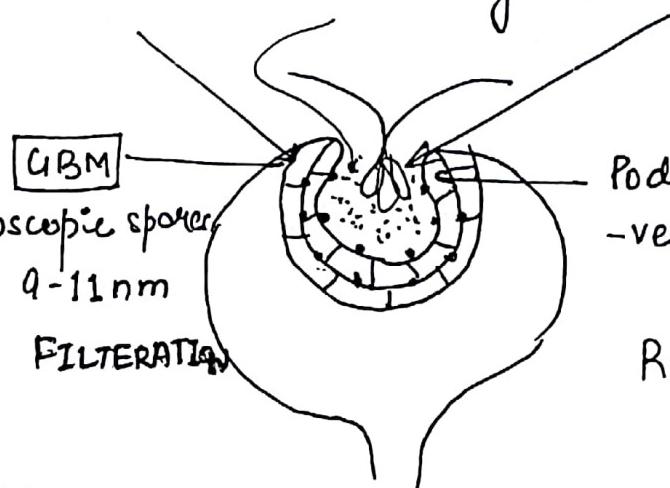


Prognosis -  
Favourable

## URINE FORMATION

1st step → Ultrafiltration → Glomerulus

Intra-GBM ← Mesangium → outside GBM. (extra-GBM)



a) All Blood Components

RBCs, WBCs, platelets

b) All plasma proteins

(except albumin  $\approx 4.6 \text{ nm}$ )

① Albumin

254

② Lipoproteins

③ AT-III, Protein S, C

## GLOMERULONEPHRITIS

Predominantly affect GBM except Minimal Change Disease  
(only podocytes affected)

1) Dysmorphic Haematuria  
(MPU)

1) NO HEMATURIA

2) RBC cast - Most specific

2) Selective Proteinuria  
(albuminuria)

3) Non-selective proteinuria

3) Dyslipidaemia

4) Glomerular range proteinuria  $\rightarrow$  Hypercoagulable state  
[ $\geq 2 \text{ g/day} / 1.73 \text{ m}^2$ ]

## TUBULES

Reabsorption + Secretion. (concentrating Ability)

Mechanisms:- Tubular transport

A) cellular transport

(across the cell)

B) Paracellular

(in bet' cells of tubule)

1) ACTIVE  $\rightarrow$  ATPase pumps.

PCT

DCT

2) PASSIVE  $\rightarrow$  exchange/  
co-transporter.

Leaky Epithelia

Tight Junctions

Allows BULKY  
Transport

Highly regulated

# DCT

URINE

H<sup>+</sup> secretion  
(most potent)

secretion

Ca<sup>2+</sup>/Mg<sup>2+</sup>

Hypercalciuria

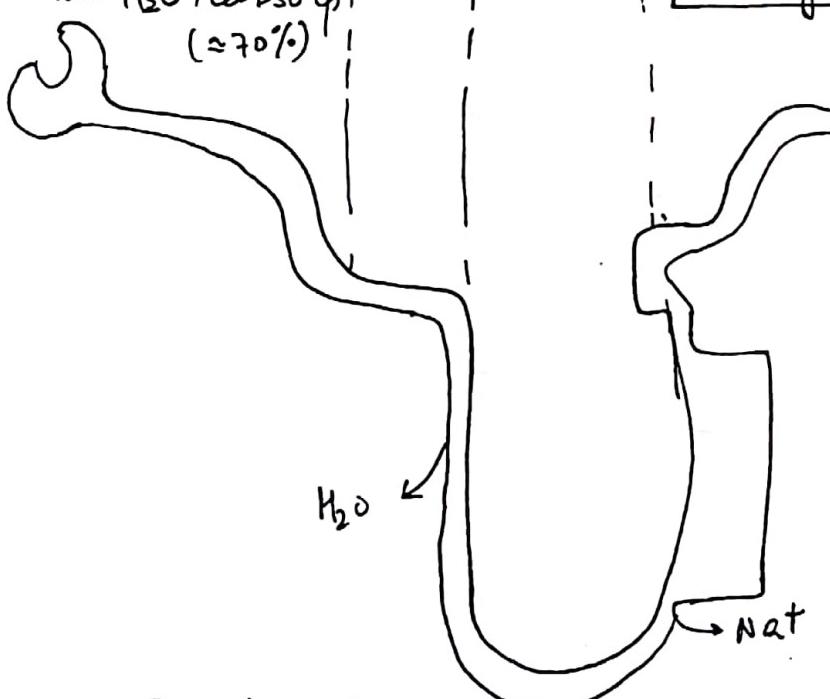
④ Hypocitraturia  
(unknown mech.)

ROLE: WATER BALANCE

PCT

Max. H<sub>2</sub>O reabsorp<sup>n</sup>  
(≈ 70%)

LoH



ADH (vasopressin)

V<sub>2</sub> receptors

AQUAPORIN channels



facilitates H<sub>2</sub>O reabsorp<sup>n</sup>



Restores plasma volume

# BODY

255

Chro. acidemia

Mild Hypokalemia

mild Hypomagnesemia

association = endocrine

Det & CD ⇒  
always Hypo-osmole

FINAL OSM  
(Based on  
fluid status)  
↓  
If Dehydrated

Aldosterone (mineralocorticoid)

↑  
upregulates eNa<sup>+</sup> channels.

( $\leftrightarrow$ )  
↓  
Na<sup>+</sup> reabsorp<sup>n</sup> Secretes  
H<sub>2</sub>O " " H<sup>+</sup>, K<sup>+</sup> in  
exchange

|                                               |                              |                                                   |                                                                         |
|-----------------------------------------------|------------------------------|---------------------------------------------------|-------------------------------------------------------------------------|
| Defn:<br>Hypotonic Polyuria<br>(D. Insipidus) | Excess:-<br>Oliguria (SIADH) | Defn:<br>Addison's<br>(AC + MC Def <sup>-</sup> ) | Excess:-<br>Conn's<br>(CUSHING's Syn.)<br>↓<br>Hypokalemic<br>Alkalosis |
|-----------------------------------------------|------------------------------|---------------------------------------------------|-------------------------------------------------------------------------|

## HYPOKALEMIC ALKALOSIS

Due to aldosterone excess state

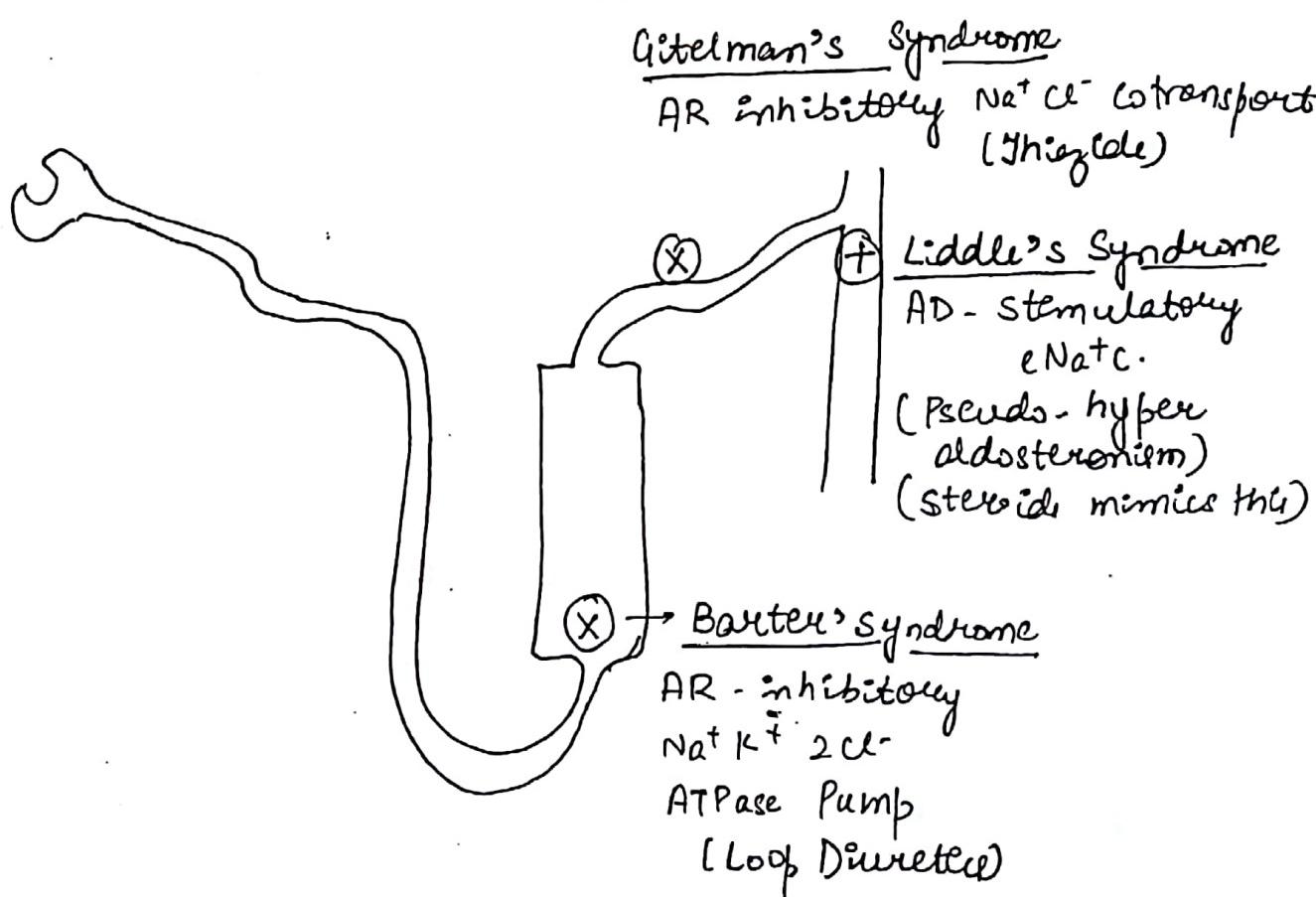
Causes: → Endocrine (MIG)

2) Chronic Drug use

- Loop Diuretics
- Thiazides
- Steroids

3) Inherited Channelopathies

## INHERITED CHANNELOPATHIES



Bartter's  
Syndrome

(6 genetic mut<sup>n</sup>)

1) **Repid** → I.U.L → adolescence.

2) **Patho** →  $\text{Na}^+ - \text{K}^+ - 2\text{Cl}^-$  pump  
 $\times \times \times$  - severe

3)  $\times \times \times \text{H}_2\text{O}$  reabsorp<sup>n</sup>

4) **Plasma volume** ↓ ↓ ↓

5) **B.P.** ↓ ↓ ↓

6) **Renin** ↑ ↑ ↑

Angiotensin

Aldosterone ↑ ↑ ↑

7) **Associated Defects**  
(Unknown) mech  
30% - SNHL (Deaf)  
Paracellular  $\text{Ca}^{2+}$  transport defect  
(Hypercalcemia)

8) **C/F** →  
1) Polyhydramnios  
2) Failure to thrive  
3) Hypotension (syncope)  
4) Renal calculi

9) **ABG analysis**

10) **S. K<sup>+</sup>**

Hilteman's  
Syndrome

20 - 30 yrs

$\text{Na}^+ - \text{Cl}^-$  cotransport

$\times$  Mild

$\times$   $\text{H}_2\text{O}$  reabsorp<sup>n</sup>

↓

~~N~~ (N)

↑

↑

Paracellular  $\text{Mg}^{2+}$  transport Defect

Muscle cramps  
Paralytic ileus  
Cardiac arrhythmias

Pseudo-hyper aldosteronism.

Asymptomatic  
Detection - HTN  
in young

LIDDLE's Syndrome  
257

20 - 30 yrs.

e $\text{Na}^+$  c

$\oplus$  Mild

$\oplus$   $\text{H}_2\text{O}$  reabsorp<sup>n</sup>

↑

↑

↓ ↓ ↓

↓ ↓ ↓

Metabolic alkalosis.

Low

|                                           |                             |                                                                                    |                                                                                                               |
|-------------------------------------------|-----------------------------|------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------|
| 10) Exclude chro. use                     | Loop Diuretics              | Thiazide                                                                           | Steroids <del>258</del>                                                                                       |
| 11) Best Test<br>S. Renin                 | ↑↑↑                         | ↑                                                                                  | ↓↓↓                                                                                                           |
| 12) <input checked="" type="checkbox"/> R | HYDRATION                   | K <sup>+</sup> supplements<br>Mg <sup>2+</sup> supplements<br>↓ minimises symptoms | <del>AMILORIDE<br/><u>DOC</u></del><br>ENaC antagonist<br>Safe in ♂<br>Long term use offers cure<br>BEST Prog |
| 13) Prognosis                             | <b>[WORST]</b><br>(no cure) | Favourable                                                                         |                                                                                                               |

## ROLE OF KIDNEY IN ACID BASE BALANCE

Human Body → "Pro-~~acidic~~ acidic state"

Every living cell requires energy (ATP)

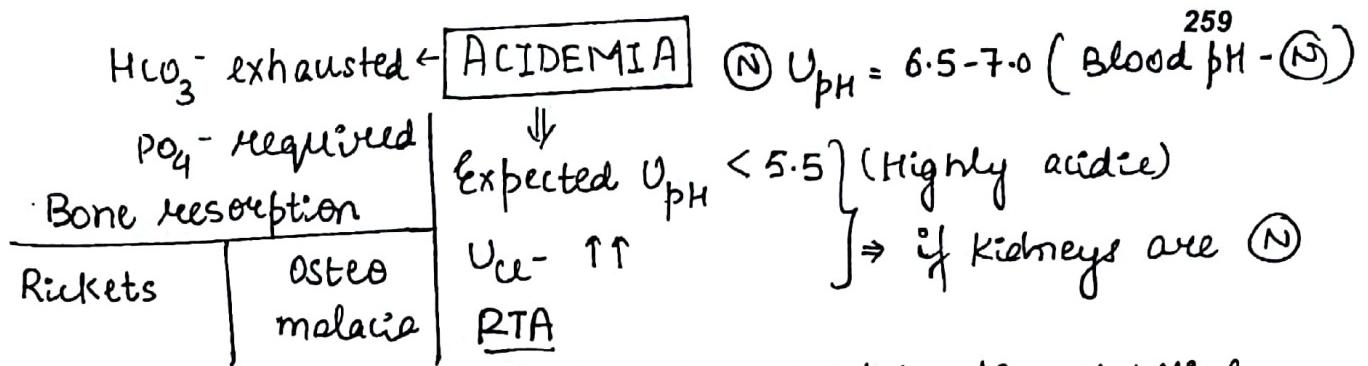
During ATP Production → Acid is ~~generated~~.

(N) pH = 7.35 - 7.45 (slightly Basic)

MECHANISMS → ABB → Regulate pH efficiently

| 1) Buffering                                                                   | Respiratory mechanism                                              | Renal Mechanism                                                                                                                     |
|--------------------------------------------------------------------------------|--------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------|
| At tissue level<br>$\text{HCO}_3^-$ ( <u>extra cellular</u> )                  | <u>BACKUP</u><br>$\text{PO}_4^{2-}$<br>(Intra cellular)<br>(Bones) | excretes acid in form of $\text{CO}_2$                                                                                              |
| $\downarrow$                                                                   |                                                                    | Most Potent<br>↓<br>Acidification of Urine                                                                                          |
| $[\text{H}^+] + [\text{HCO}_3^-] \rightarrow \text{CO}_2 + \text{H}_2\text{O}$ |                                                                    | Most Imp. form of $\text{H}^+$ Secretion in urine → $\text{NH}_4^+$ ion.<br>Combines $\text{Cl}^- \rightarrow \text{NH}_4\text{Cl}$ |

$V_{H^+}$  &  $V_{Cl^-}$  levels.



Defect in acidification of urine  
( $U_{pH} > 5.5$ ,  $U_{Cl^-}$  - Low in disease)

RTA

①  $H^+$  secretion

$H^+ - K^+$  ATPase



④ Minor role

Aldosterone  
 $H^+ / K^+$  secretion.  
in exchange of  
 $Na^+ + H_2O$ .

②  $HCO_3^-$  reabsorb?

$HCO_3^-$  reabsorb?  
( $H_2O$ -nutrient  
reabsorb?)

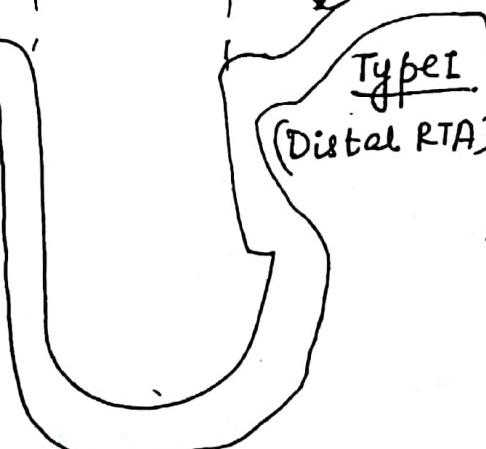
③  $HCO_3^-$  regeneration  
(Action - carbonic  
anhydrase)

⑤ Type 2 RTA  
(proximal RTA)

$< 100$  cases (worldwide)

Majority :- cerebral calcification.  
also - marble bone disease  
(osteopetrosis)

Not included in routine classification.



⑥ Type 4 RTA  
(Hyper acidosis)

| <u>RTA</u>        | <u>Type I</u>                                                                                                                                             | <u>Type II</u>                                                                                                                           | <u>Type IV</u><br>260 M/C RTA                                                                         |
|-------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|
| epidemiology.     | <10yr, M>F<br>(Most <del>per</del> severe)                                                                                                                | 20-30yr<br>M=F<br>(mild)                                                                                                                 | >50yr, M=F<br>(Mildest)                                                                               |
| M/C inherited RTA | Inherited                                                                                                                                                 | Inherited                                                                                                                                | M/C RTA                                                                                               |
| Cause             | Inherited                                                                                                                                                 | Inherited                                                                                                                                | Mildest<br>(Acquired)                                                                                 |
| Association.      | <p>30% autoimmune</p> <p>M/c - Sicca syndrome</p> <p>SLE</p> <p><u>M/c TINU</u></p> <p>Mixed connective tissue disorder</p>                               | <p>FANCONI'S syndrome:</p> <ul style="list-style-type: none"> <li>- glycosuria</li> <li>- aminoaciduria</li> <li>- syndactyly</li> </ul> | <p>Early CKI.</p> <p>ACEI/ARB</p> <p>K<sup>+</sup> &amp; par. diurekt.</p> <p>Tetraethylammonium.</p> |
| C/F               | <p>① short stature, Rickets</p> <p>② Hypercalcemia<br/>↓ St-one<br/>↑ Renal calculi<br/>Nephrocalcinosis</p> <p>③ Hypomagnesemia<br/>↓<br/>M/s cramps</p> | <p>① mild acidemia<br/>Asymptomatic</p> <p>② Vit D<sub>3</sub>/PO<sub>4</sub> def.<br/>(2° to loss in urine)<br/>↓<br/>osteomalacia</p>  | <p>① mild acidemia</p> <p>Asymptomatic</p> <p>② Rarely<br/>Hyper K<sup>+</sup><br/>complications</p>  |
| ABG analysis.     | Metabolic Acidosis                                                                                                                                        |                                                                                                                                          |                                                                                                       |
| Anion gap         | (N) anion gap                                                                                                                                             |                                                                                                                                          |                                                                                                       |
| V <sub>AG</sub> . | $(U_{Na^+} + U_{K^+}) - U_{Cl^-}$ [High/Positive]                                                                                                         |                                                                                                                                          |                                                                                                       |
| V <sub>pH</sub>   | always<br>>5.5                                                                                                                                            | maybe <5.5                                                                                                                               | always<br>$\odot$<br><5.5                                                                             |

S. K+

Low

(N)

High

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Rx

Oral  $\text{HCO}_3^-$  supp.

Oral  $\text{K}^+$

Citrate supp.

↓ Renal calculi

(No cure)

Vit D<sub>3</sub> / P<sub>o4</sub>  
supplements

↓ Bone Disease

X

Stop offending drug  
↳ offers cure.

Prog.

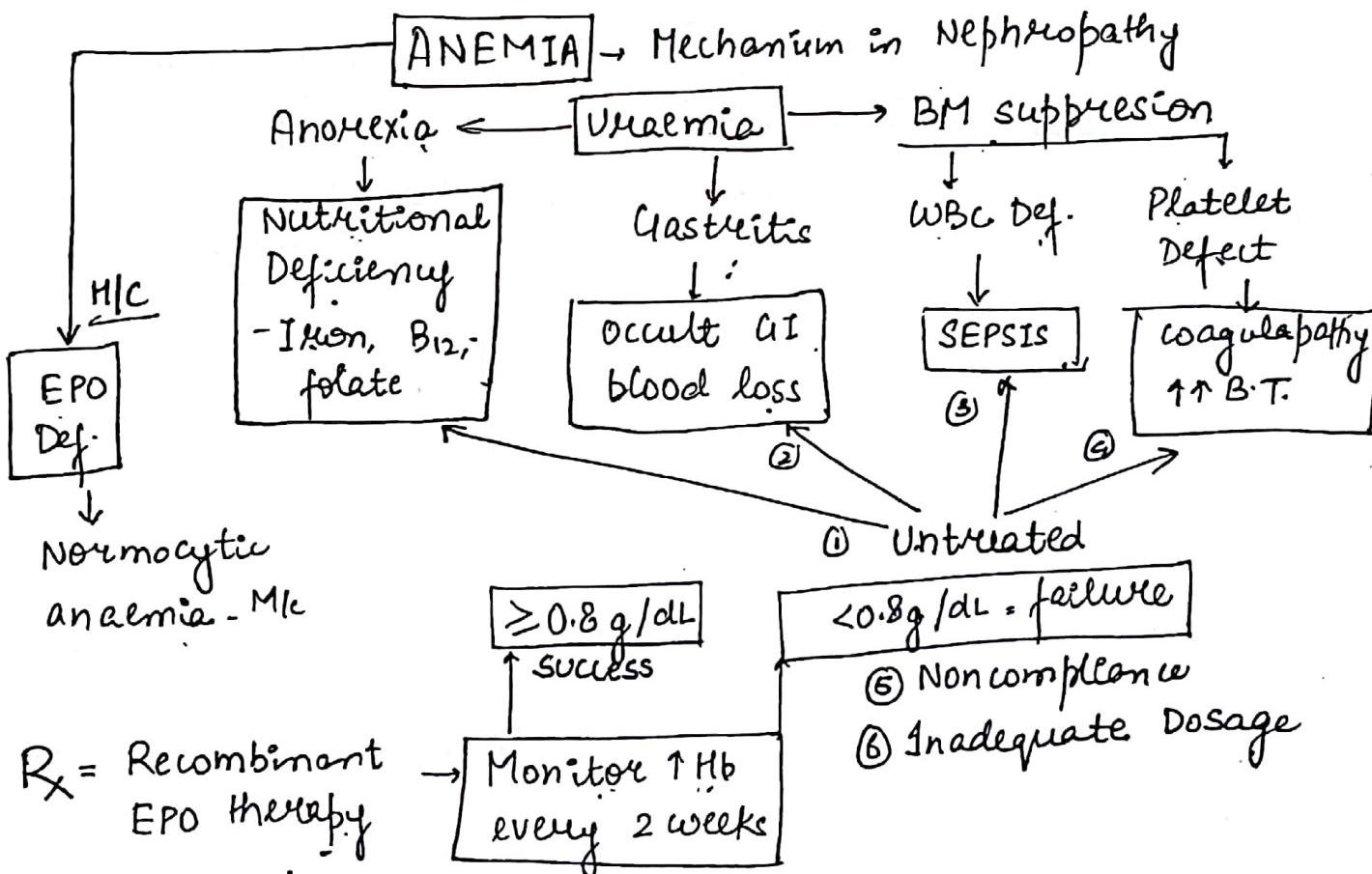
WORST

Favourable

BEST

## ANEMIA

Defect in Erythropoietin Synthesis



Vit D → final step of activation into **Vit D<sub>3</sub>**  
 & its reabsorption occurs in **PCT**

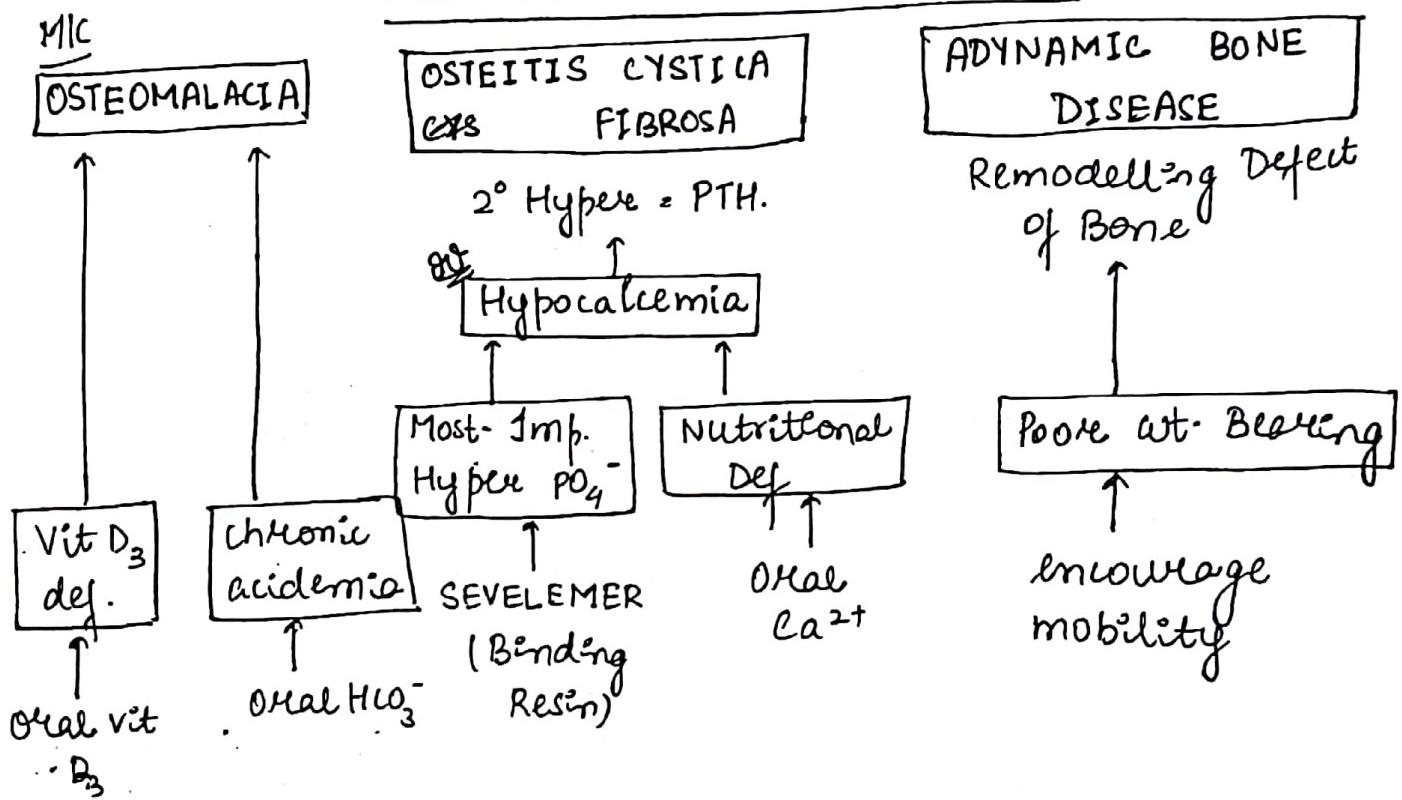
262

↓ if defective

BONE DISORDERS - in nephropathy

only C.K.I - Minimum ( $\geq 6$  months) disease

## RENAL OSTEODYSTROPHY



## ASSESSMENT METHODS IN NEPHROLOGY

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### S. CREATININE LEVELS (Best) screening Test)

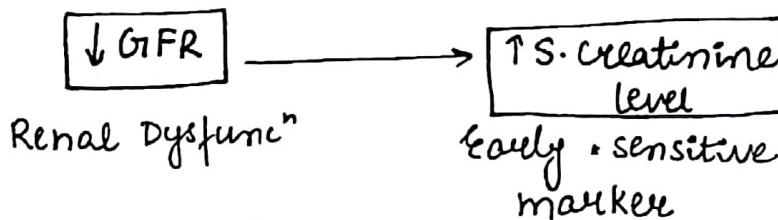
#### C PRODUCED

endogenously @ constant Rate  
By Protein Breakdown.

#### EXCRETED

freely filtered at glomerulus  
Barely secreted/reabsorbed @ tubules

$$S\text{ creatinine} \propto GFR$$



#### Limitations of Test

- nonspecific for  $\Delta$  of nephropathy.
- may not correlate immediate outcome of the disease (Limited Prognostic value)

#### FALSE +ve ↑ S. creatinine

↑ Product'

at High Protein Diet

by strenuous exercise.  
(athletes)

c) Infection (sepsis)

d) Inflammation (A.I.D.)

e) Neoplasms (some)

#### Alternative Test To S. creat

#### S. CYSTATIN - C LEVELS

Produced endogenously  
By all nucleated cells  
@ constant Rate

freely filtered @ glomerulus  
Excretion  $\propto GFR$ .

Adv - not related to Diet or exercise

NOVEL MARKERS OF AKI = specific for  $\Delta$ site of Nephropathy<sup>264</sup>

NGAL (neutrophil gelatinase associated Lipocalcin)

KIM-1 (kidney injury molecule)

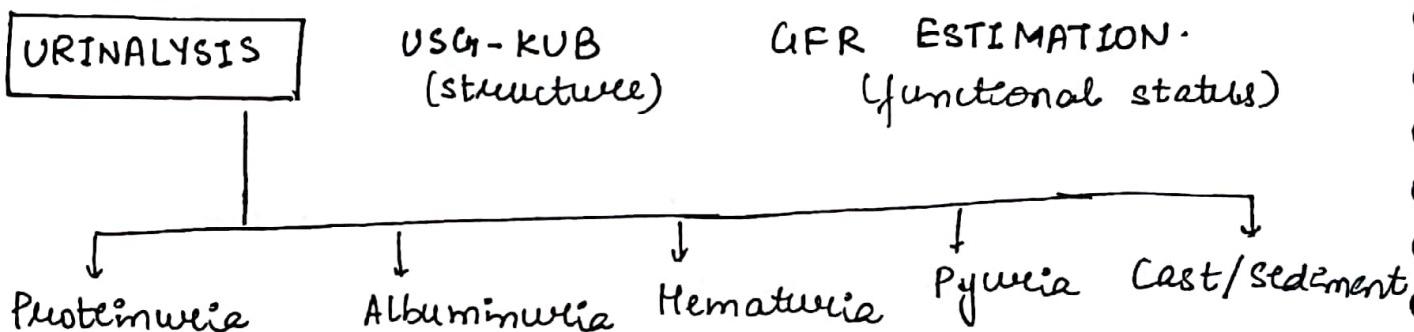
IL-18

Tested in spot urine sample

Are secreted by tubules in response to injury.

Hence detectable only in Renal causes of AKI.  
(nephropathy)

TESTS = Detect :- SITE/ CAUSE/ SEVERITY



### PROTEINURIA

Def<sup>n</sup> -  $> 150 \text{ mg/24 hours}$ .

Detected using Dipstick Method  
(very sensitive)

- Non-specific for  $\Delta$ site of Nephropathy
- Valuable in K/c/o - Nephropathy = identify SITE.  
(Based on quantity)

| $< 2 \text{ g/day}$<br>(Tubular Range) | $\geq 2 \text{ g/d} / 1.73 \text{ m}^2$ (Glomerular Range Proteinuria) |
|----------------------------------------|------------------------------------------------------------------------|
| Tubulo-interstitial<br>Disorders       | $< 3.5 \text{ g/d}$<br>Nephritic Range                                 |
|                                        | $\geq 3.5 \text{ g/d}$<br>Nephrotic Range                              |

## ALBUMINURIA

>30mg / 24 hrs

(More specific marker)

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### QUANTITATIVE TESTS

24hr urinary alb.  
estimation  
(most reliable/  
gold std)

Micro-alb

30 - 300 mg of  
Alb / 24 hrs

Gross-alb

>300mg

(Most Preferred)  
Spot urinary ACR  
(alb / creat. ratio)

30 - 300 mg of  
Alb / gm of creat

>300 mg

USE:- PROGNOSTIC  
↓  
Staging of CKD

- Early marker  
- Reversible stages  
DOC = ACEI

Late / irreversible  
stages

## Approach → HEMATURIA (RBC in urine)

Step 1 - Establish "SIGNIFICANT" (any +) "INSIGNIFICANT"

- $> 3-100 \text{ RBC/hpf} \geq 3 \text{ occasions}$  only observation.
- $> 100 \text{ RBC/hpf}$  single occasion. Repeat after 48 hrs
- GROSS HEMATURIA



### Step 2 - Urine microscopy : RBC morphology in urine

| EUMORPHIC                       | DYSMORPHIC<br>(SOURCE → Renal)<br>Disease → GN | GROSS H.<br>Microscopic Hematuria                        |
|---------------------------------|------------------------------------------------|----------------------------------------------------------|
| Source - Below the Renal Pelvis |                                                |                                                          |
| Renal calculi                   | IgA nephropathy                                | Post-infective<br>causes                                 |
| Cystitis                        |                                                | Post-streptococcal<br>GN (PSGN)                          |
| Carcinoma bladder               |                                                | Hep B - Polyarteritis Nodosa                             |
| ↓                               |                                                | Hep C - Cryoglobulinemia<br>SABE                         |
| <b>Radiological Testing</b>     |                                                |                                                          |
| X-Ray                           |                                                |                                                          |
| USG                             | KUB                                            |                                                          |
| CT                              |                                                |                                                          |
| ↓                               |                                                |                                                          |
| Inconclusive                    |                                                |                                                          |
| ↓                               |                                                |                                                          |
| <b>Cystoscopy ± Biopsy</b>      |                                                |                                                          |
|                                 | NORMAL                                         | $C_3 = \text{initially Low}$<br>Returns to (N) - 6-8 wks |
|                                 |                                                | Persistently<br>Low<br>complement<br>levels              |

## Approach - PYURIA. (Pus/WBC in urine)

Step 1 : "SIGNIFICANT"  $> 5 \text{ WBC/hpf}$  in centrifuged sample → observe/Repeat if not significant

## Step 2 :- URINE CULTURE.

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H/c cause of significant pyuric = UTI.



### **STERILE PYURIA**

#### CAUSES

Infective

M/c - Partially Rx UTI.

(>72 hrs antibiotic)

FASTIDIOUS ORGANISMS

(special growth requirement)

Chlamydia

M/c of STD

♀

Renal T.B.

Inflammatory

1) Renal Calculi

2) **Papillary Necrosis**

(severe tubular necrosis)

Vascular insufficiency - Mech.

DM - analgesic abuse

Sickle - Kawasaki Disease

3) Post - Radiotherapy

4) Post - Transplant Rejection.

#### Approach :- CASTS / SEDIMENTS

Common CASTS

But non-specific  
for Diagnosis

M/c cast in urine

HYALINE CAST

Most Benign cast

NO further Rx / test

M/c found in AKI.

M/c cast in nephropathy

GRANULAR / CELLULAR

Present in (B)

Tubulo-interstitial GN

RARE CASTS

(10-15% case)

RBC cast

WBC cast

Muddy Brown Cast

Eosinophilic Cast

Broad/waxy Cast ↑

WORST CAST

DIAGNOSTIC

GN \* (Acute GN)

Pyelonephritis

Acute Tubular Necrosis

Acute Interstitial Nephritis

C.K.I.\*

Indicates total break down of tubules.

## USG - KUB

268

(N)

1) SITE :- Anatomical

2) SIZE :- 7-11 cms

< 7cm (shrunken)

CKI (exception)

Ab (N) & its Interpretation

ECTOPIC → NO relation to function

> 11 cms - Enlarged / Bulky

AKI. → classical in acute Interstitial Nephritis

Early DM nephropathy

Adult PKD (APKD)

HIV associated Nephropathy

Renal Amyloidosis

3) SYMMETRY < 1.5 cms

> 1.5 cms - assymmetrical kidneys.

Pathology ⇒ always in smaller kidney

4) ECHOTEXTURE = (N)

Increased echogenicity

↓  
Active Disease in the Kidney

5) Cortico-Medullary Differentiation (CMD)

Most Imp. parameter

AKI

(Vs)

CKI

Preserved

Loss

6) COLLECTING SYSTEM - (N)

Obstructive uropathy

## GFR ESTIMATION (Functional status)

269

- Most preferred = (Creat. clearance  
(Indirect/ surrogate marker))  
Easy, cheap, no radiation expo
- Cockcroft Gault formulae  
(Estimated)

$$eGFR = \frac{[140 - \text{Age}] \times \text{wt(Kg)} (\delta^7)}{72 \times \text{s.creat}}$$

$$- [ ] \times 0.85 \quad \text{♀}$$

### Dilad

- Inaccurate (esp in AKI)
- only - total Kidney GFR

### Most Reliable/Gold Std :-

- Radio-isotope scan.  
(DTPA, MAG-3)
- Direct method.
- Accurate
- Single Kidney GFR
- Segmental GFR.
- Total Kidney GFR.

### Dilad

- Invasive
- Expensive
- Radiation exposure

### Uses - MEDICAL

- Staging of CKD
- Follow-up - chronic medical Renal Disease  
e.g. DM, HTN, HIV associated Nephropathy
- Dose adjustment of Nephrotoxic drugs

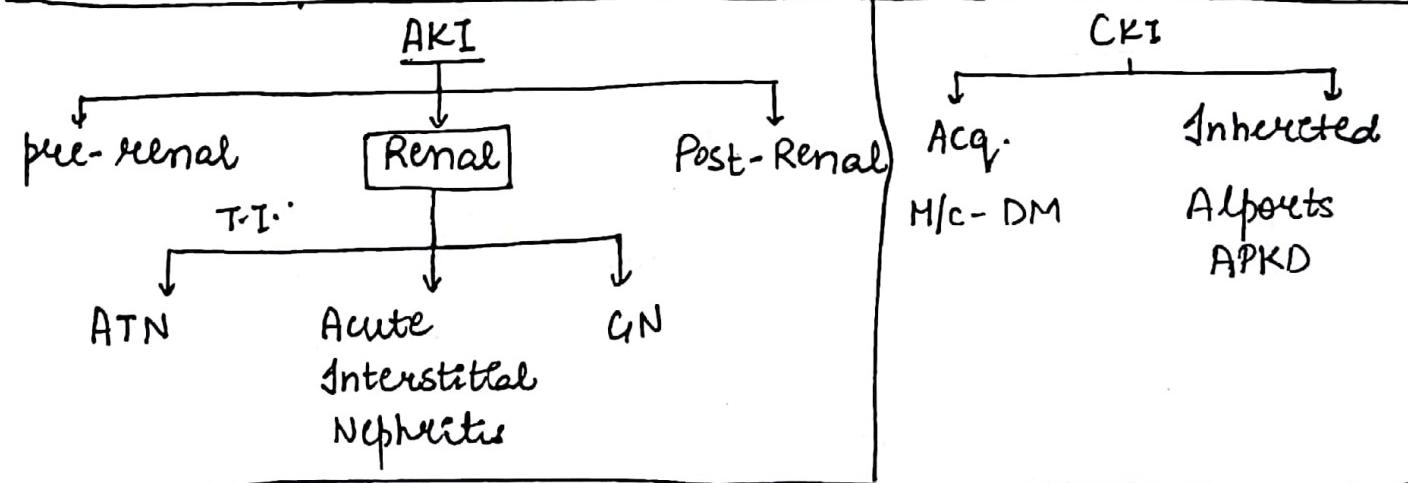
### Uses

- Pre-Transplant assessment of DONOR
- Pre-op assessment of w~~oss~~
- Medicolegal
- Decision making
  - to operate on better kidney  
never done B/L → risk of infection ↑

## INDEX : RENAL DISORDERS

270

| <u>AKI</u>        | <u>Parameters</u>       | <u>CKI</u>      |
|-------------------|-------------------------|-----------------|
| Preserved         | USG = CMD               | Lost            |
| (N) or ↑          | USG - size              | (N) or ↓        |
| Fluctuates - Posm | Osmolarity              | Isothenuria     |
| Hyaline cast      | CASTS                   | Broad waxy cast |
| (-) uncommon      | Anaemia                 | (+) common.     |
| uncommon.         | Renal<br>Osteodystrophy | (+)             |



R.R.T (Renal Replacement Therapy)

## AKI

Def<sup>n</sup>: Abrupt decline in GFR over short period of time<sup>27</sup>

KDIGO Guidelines (Kidney disease improving Global outcome - part of National Kidney Found<sup>n</sup>)  
Any 1

- ↓ U.O.  $\leq 0.5 \text{ mL/kg/h}$   $\geq 6 \text{ h}$  (oliguria).
- ↑ S.Cr.  $\geq 0.3 \text{ mg/dL}$  from Baseline  $\leq 48 \text{ h}$
- ↑ S.Cr.  $\geq 1.5 \times \text{Baseline}$   $\leq 7 \text{ days}$ .  
(50% increase)

### Causes of AKI

#### Pre-Renal

60-85% - HYPOPERFUSION

#### 1) Dehydration

Diarrhoea

Hypoalbuminemia

Massive H<sup>2</sup>O loss

Burns

(Insensitive losses through skin)

#### 2) Hypotension

Cardiogenic

Septic shock.

#### 3) Drugs - disrupt autoregulation.

#### Renal

#### INTRINSIC

95%

Tubulo  
Interstitial  
Disorders.

5%

GN

#### Post-Renal

1-5% - OBSTRUCTIVE  
UROPATHY

C/F

PR

Classical 3 stages

Oliguria <400mL/d

Anuria <100mL/d

Diuretic phase (recovery)

Renal

1) Non-Oliguric AKI

e.g. SEPSIS

(In Tubulo-Interstitial)

2) Hematuria - GN

Post-R

Loin pain<sup>272</sup>

Dysuria

Urgeency

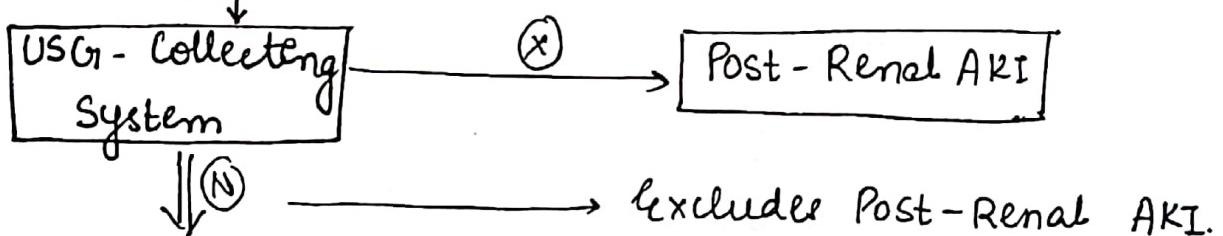
Rarely - Serious UREMIC MANIFESTATIONS

(cause - mortality in A.K.I.)

- 1) Encephalopathy / convulsion
- 2) Pericarditis / shock
- 3) Coagulopathy

ASes → KDIGO Guidelines.

Approach - AKI



| PARAMETER                      | PRE-RENAL                                                                              | RENAL                                                              |
|--------------------------------|----------------------------------------------------------------------------------------|--------------------------------------------------------------------|
| MECHANISMS                     | RAAS +<br>↓<br>Na <sup>+</sup> /H <sub>2</sub> O reabsorption<br>↑ Urate reabsorption. | Loss of concentrating ability<br>Nat lost in urine<br>Dilute urine |
| BUN : Creat.                   | >20:1                                                                                  | <12:1.                                                             |
| U <sub>Na</sub>                | <20mEq                                                                                 | >40mEq                                                             |
| F <sub>e</sub> Na <sup>+</sup> | <1%                                                                                    | >2%                                                                |

|                                                 |               |                                   |
|-------------------------------------------------|---------------|-----------------------------------|
| U <sub>osm</sub>                                | > 500 mosm/L  | < 350 mosm/L                      |
| CASTS                                           | Hyaline casts | Granular/ <sup>273</sup> cellular |
| USG- Echotexture                                | (N)           | ↑ / Bright kidney                 |
| <u>Single Best<br/>Novel markers of<br/>AKI</u> | UNDETECTABLE  | DETECTABLE                        |

### Rx PALLIATIVE

#### Indications of Dialysis

- 1) UREA > 100
- 2) CREAT > 7
- 3) SERIOUS UREMIC MANIFESTATIONS
- 4) Refractory Pulmonary edema
- 5) Hyperkalemia > 6.5 mEq
- 6) Refractory pH < 7.20

Single most imp. Indication for emergency Dialysis

#### 7) Ingested Dialysable Toxin

(commonly med. Accidental/suicidal)

a) Salicylates

b) Methanol

c) Lithium

d) Polyethylene glycol (solvent)

### SPECIFIC

Depends on cause

#### (A) Post- Renal AKI

Early Sx relief  
Excellent recovery

#### (B) Pre- Renal AKI

Fluid challenge (1st Line)

Inotropes

Antibiotics

Stop offending drug

Excellent recovery

Delay in Rx  $\Rightarrow$  Progress to ATN

#### (C) RENAL AKI.

↓  
Further evaluation.

## Approach - RENAL AKI

95%

5%

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| Tubulo-Interstitial | Parameters  | CIN     |
|---------------------|-------------|---------|
| <2g/day             | PROTEINURIA | >2g/day |
| (-)                 | HEMATURIA   | common. |
| Granular            | CASTS       | RBCs.   |

T. I.  $\Rightarrow$

| ATN         | Parameters         | Acute Interstitial Nephritis |
|-------------|--------------------|------------------------------|
| >4%         | Fe Na <sup>+</sup> | 2-4%                         |
| (+)         | USG - size         | enlarged / Bulky             |
| Muddy Brown | CASTS              | Eosinophilia                 |

### ATN (Tubule - M/c site)

#### Anatomy

Prone to  
vascular  
Insufficiency

#### Physiology

Site of conc<sup>n</sup>

#### Direct

Luminal  
Contents

- 1) Untreated Pre-renal
- 2) Sepsis
- 3) Contrast Induced Nephropathy
- 4) Drugs - aminoglycosides
- 5) Toxins - Heavy metal poison.
- 6) Cryoglobulinemia
- 7) Myoglobinuria
- 8) Hemoglobinuria

### AIN

- 1) Allergic Response to Drug (M/c - 95% of case)  
NSAIDs  
Sulfonamides  
Penicillin.  
cephalosporin  
Rifampicin  
FQs  
Dapsone  
Nitrofurantoin  
Contrast agents.
- 2) Viral infec
- 3) autoimmune
- 4) Lympho-proliferative

|                    |                  |                              |
|--------------------|------------------|------------------------------|
| Supportive therapy | Rx               | stop offending Drug          |
| Underlying cause   |                  | supportive Rx <sup>275</sup> |
| 4-6 wks            | Avg.<br>Recovery | 1-2 wks                      |
|                    |                  | < 1 %                        |
| 1-5 %.             | Risk of ESKD     |                              |
| Favourable         | Prognosis        | GOOD                         |

## GLOMERULONEPHRITIS

Causes :-

(A) PATHOLOGICAL :- Mesangial Involvement on Biopsy

(+) Proliferative GN

• Mesangio-proliferative GN  
(IgA, PSGN)

• Crescentic GN (worst Prog)  
(RPGN)

• Membrano-proliferative GN  
MPGN - mesangio-capillary

(-) Non-Proliferative GN

- Minimal Change Disease
- FSGN
- Membranous nephropathy

(B) CLINICAL PRESENTATION of GN (More Preferred)

| Asymptomatic proteinuria<br>microscopic hematuria<br><br>(M/c) | Nephritis<br>→ Hematuria<br>→ HTN<br>→ Rapid ↓ GFR.<br>(M/c - RPGN)<br>→ Proteinuria<br>< 3.5 g/day | Nephrotic<br>→ Anasarca<br>(serous cavity)<br>→ Hypercoagulable State<br>→ Preserved GFR<br><br>GFR<br>> 3.5 g/day<br>1.73 m <sup>2</sup> | Reno-vascular HTN | C.K.I<br>eg. Alport's Syndrome |
|----------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------|-------------------|--------------------------------|
|----------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------|-------------------|--------------------------------|

## Nephritic

- PSGN
- Lupus nephritis
- RPGN

## Nephrotic

children → MCD

Adults → FSGS

Elderly → membranous  
(> 50 yrs) nephropathy

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### Proliferative GN

### Non-Proliferative

More likely nephritic

More likely nephrotic

## MESANGIO-PROLIFERATIVE

### IgA nephropathy

Worldwide

M/c cause

### PSGN

India

Epidemic

20-30 yrs, ♂ = ♀

5-15 yrs. ♂ = ♀

Etiopath

← Post-infective

M/c preceded by URTI →

Latent Period

< 1<sup>st</sup> week

1-3 weeks

SKIN

Syn-pharyngitic

4-6 weeks

C/F

Recurrent Gross Hematuria

Microscopic hematuria

10-15% - Persistent microscopic

Common  
[clawed nephritis syndrome].

Screening (Serology)

S. IgA - I level ↑↑

Anti-DNAase (70% case +)  
ASO, anti-hyaluronidase

Serum complement

(N)

Initially Low  
Returns to (N) in 6-8 weeks

WhatsApp: +1 (402) 235-1397

|                                |                                                                                                                                                                     |                                                                                                                                                                                            |
|--------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <u>Biopsy</u>                  | Mesango- Proliferative changes                                                                                                                                      | 277                                                                                                                                                                                        |
| <u>Immuno<br/>fluorescence</u> | Granular Pattern of Ig deposits                                                                                                                                     |                                                                                                                                                                                            |
|                                | Anti IgA staining                                                                                                                                                   | Anti IgG Staining                                                                                                                                                                          |
| Rx                             | <ul style="list-style-type: none"> <li>Reassurance</li> <li>Majority - self Limiting</li> <li>Risk of RPGN <math>\leq 1\%</math></li> <li>Plasmapheresis</li> </ul> | <ul style="list-style-type: none"> <li>Penicillin - no role in nephropathy</li> <li>To eradicate residual. Infe.</li> <li>Long Term prophylaxis.</li> <li>(X) Low relapse rates</li> </ul> |
| Prognosis                      | BEST among GN                                                                                                                                                       | 2nd Best (Risk of RPGN 1-5%)                                                                                                                                                               |

### POOR PROGNOSTIC FACTORS

- 1) Elderly onset ( $> 40$  yrs)
- 2) Nephrotic
- 3) Progression to **RPGN** — any GN requires RRT  
 $\leq 1$  month of onset

### LUPUS NEPHRITIS

Kidney involvement - most dreaded.

organ involvement in SLE  $\rightarrow$  H/c/c of acute mortality

Deposition of Anti-dsDNA on GBM. (100% specific)

| Type | PATHOLOGY                        | C/F                                                            | Rx           |
|------|----------------------------------|----------------------------------------------------------------|--------------|
| I    | Minimal Mesangial proliferation. | Asympt - Proteinuria<br>microscopic Hematuria<br>Preserved GFR | No active Rx |
| II   | Diffuse mesangial proliferation. |                                                                |              |

|     |                      |                              |                                  |
|-----|----------------------|------------------------------|----------------------------------|
| III | Focal nephritis      | Classical nephritic syndrome | I.v. methyl prednisolone therapy |
| IV  | Diffuse nephritis    | High risk - RPGN (15-20%)    |                                  |
| V   | MPGN/membranous      | Nephrotic Synd.              | oral steroids                    |
| VI  | Glomerular-Sclerosis | CKI                          | consider RRT                     |

RPGN  $\rightleftharpoons$  Crescentic GN  
 (Clinical Asx) (Biopsy pending)

### APPROACH - RPGN

| Anti GBM Ab                                                                                                                                            | ANCA                                                                                                       | Serum. Complement levels                                                                                                                            |
|--------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|
| <u>GOOD PASTURE'S Syndrome</u><br>Autoimmune (GPS)<br>20-40 yrs ♂ > ♀<br>$\alpha_3$ subunit - Type 4 collagen<br>Goodpasture's Ag<br>Alveolar BM   GBM | <u>Vasculitis</u><br>mimics GPS<br>So, D/D. for Pulmonary-Renal Syndrome<br>- Wegener's<br>- Churg-Strauss | <u>Low C<sub>3</sub></u><br>↓ Anti dsDNA<br>Lupus (SLE)<br>  ⊥ Anti-DNAase<br>PSGN<br>↓ ⊥ HbsAg<br>PAN<br>HCV-Ab<br>Cryoglobulinemia<br>↓ ECHO-SABE |
| (Pulmonary   Renal Syndrome)<br>Alveolar H'ge   RPGN<br>↓<br>Mc among smokers.                                                                         | - microscopic polyangiitis (MPA)<br>Sparse Ig deposits (pauci-immune)                                      | (N) C <sub>3</sub><br>Ig A<br>Henoch-Schonlein Purpura                                                                                              |
| I.F. :- Linear pattern of Ig deposits                                                                                                                  |                                                                                                            |                                                                                                                                                     |
| Rx $\leftarrow$ PLASMAPHERESIS                                                                                                                         |                                                                                                            | Plasma pheresis                                                                                                                                     |
| Pronosis $\leftarrow$ POOR > 70% acute mortality $\rightarrow$                                                                                         |                                                                                                            | Poor Prog.                                                                                                                                          |

# MPGN

Biopsy Based A.S.  
30-50 yrs.  
 $\sigma > \varphi$

279  
70% cases  $\rightarrow$  Low C<sub>3</sub> Level

90% causes  $\rightarrow$  2° causes

## causes

- 1) Infections - Leprosy  
Malaria  
Syphilis  
Hep. B  
Hep. C

- 2) Autoimmune - Type II MPGN Lupus nephritis

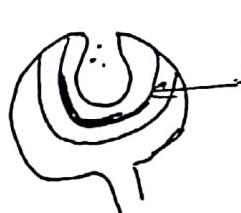
- 3) Solid Organ Tumours - [H/c Renal manifestation = MPGN]

- 4) Lymphoproliferative states

## C/F

Majority  $\rightarrow$  "NEPHROTIC SYNDROME"

A.S. Renal Biopsy - Double BM /  
Thickened appearance of GBM.  
[Only INTRA-GBM MESANGIAL involvement]  
 $\hookrightarrow$  causes splitting of GBM.



10% Idiopathic  $\rightarrow$  Rx - Immunosuppressants

| FS GNS<br>(M/c - adults)                                   |                                                       | MEMBRANOUS NEPHROPATHY<br>(M/c > 50 yrs)<br>280                                                              |
|------------------------------------------------------------|-------------------------------------------------------|--------------------------------------------------------------------------------------------------------------|
| 1° (idio)<br>M/c Biopsy findings = sclerosing type of FSGS | 2° causes<br>end point of DM<br>HTN<br>Reflux induced | 85%<br>1° (idio)<br>EM findings (Gold std)<br>Spike & Dome appearance of GBM<br>2° causes<br>Same as in MPGN |
| Most Severe<br><u>Collapsing</u> type of FSGS              | HIV associated nephropathy                            |                                                                                                              |
| C/F - HTN<br>Early & severe features                       |                                                       | <b>NEPHROTIC</b> WORST Hypercoagulable state<br>Hence, max. risk → RV thrombosis.                            |
| Rx underlying disease + strict HTN control                 |                                                       | Anti-coagulation (all cases) + Immunosuppressants                                                            |
| Risk of ESRD                                               | Common - slow<br>15-20 yrs                            | Common - 5-10 yrs                                                                                            |
| Acute mortality                                            | No                                                    | Favourable Prognosis<br>Present (vascular)                                                                   |
|                                                            |                                                       | WORST PROG.                                                                                                  |

# C.K.I.

281

Gradual ↓ GFR ≥ 3 months duration.

Kidneys → Large functional Reserve.

|                  |                        |                     |
|------------------|------------------------|---------------------|
| Clinical Disease | ≥ 70% Loss of nephrons | ≈ 25-40 mL/min eGFR |
|------------------|------------------------|---------------------|

C/F -

1) UREMIC Symptoms (M/c) → M/c neurological feature (90%)

- Encephalopathy / convulsions
- Pericarditis / shock
- Gastritis / Anorexia
- Infertility / Loss of libido
- Proximal myopathy
- Peripheral neuropathy
- Restless Leg syndrome
- Generalised pruritus

Peripheral neuropathy

- (axonal variant)
- Poor recovery despite dialysis

2) FLUID OVERLOAD symptoms

periorbital oedema

peripheral "

CHF

3) Metabolic acidosis

4) ANAEMIA - CKI

5) Renal osteodystrophy

Asy - Done

Rx STAGE of CKI

2 Parameters

Albuminuria

eGFR

Rx

282

I}

Microalbuminuria

90 - 120 mL/min

ACEI +  
strict control  
of Risk factors  
(DM, HTN)

II}

(Reversible stage)

60 - 89 mL/min

III}

Gross (irreversible  
stage)

30 - 59 mL/min

Counsel +  
Prepare for RRT

IV}

V}

Gross

15 - 29 mL/min

RRT is mand-  
atory

ESRD

< 15 mL/min  
( $\geq 90\%$  nephron  
Loss)

Specify Rx - Depends on cause.

DM  
albeto  
APKD

### DIABETIC NEPHROPATHY

Microvascular complication of DM.

Pathophysiology → Hyperglycemia ①

GLYCOSURIA = ↑ urine osm

② ↑ Glycated end products

oxidative injury  
vascular endothelial

HYPOPERFUSION

Microalbuminuria

Macroalbuminuria

↑ Glomerular capillary Pressure  
(already ③)

① ↑ GFR  
supra-④

↓ Capillary HTN

Gradual nephron  
Loss

GLOMERULOSCLEROSIS  
(F.S.G.S.)

② Return to ④

⑤ ESKD ( $> 90\%$  Loss)

| Stage                       | Duration of DM | Alb.                  | eGFR.                    | Rx                         |
|-----------------------------|----------------|-----------------------|--------------------------|----------------------------|
| I Hyper functioning         | 1-5 yrs        | -                     | Supra-N<br>> 120 mL/min. | strict DM control<br>①     |
| II Silent stage             | 5-8 yrs        | +                     | Returns to N             | Adequate Hydration.<br>+ ② |
| III Incipient (subclinical) | 8-12 yrs       | Micro albuminuria +ve | CKI stage I/II           | ACEI /ARB ③                |

Early - EM → Thickening of GBM  
non-specific to ages

|                        |           |       |               |                  |
|------------------------|-----------|-------|---------------|------------------|
| IV OVERT (symptomatic) | 12-18 yrs | GROSS | CKI Stage 3/4 | Consider RRT     |
| V ESRD                 | 18-25 yrs | GROSS | Stage 5       | RRT is mandatory |

LATE/ Advanced/EM → Nodular glomerulosclerosis  
irreversible (K-W - Kimmelstein - Wilson nodules)

## ALPORT'S SYNDROME

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H/c - X<sup>L</sup> - R defect

20-40 yrs.

♂ > ♀

$\alpha_5$  subunit - Type IV collagen = ABSENT

| H/c<br>GBM                          | Cochlear<br>B.M. | Lens                                                      | Skin                                              |
|-------------------------------------|------------------|-----------------------------------------------------------|---------------------------------------------------|
| G.N.<br>↓<br>Recurrent<br>Hematuria | SNHL             | H/c ≈ 75%<br>Dot & fleck<br>retinopathy<br>(Not specific) | Most specific<br>Ant. Lenticonus<br>(≈ 25% cases) |

4 Sy - Renal Biopsy  $\Rightarrow$  "BASKET - WEAVE" appearance  
of GBM.

only Rx - Renal Transplant:  
 $\hookrightarrow$  Never recurs in graft  
excellent survival

Post-Transplant Complication - Mimic Recurrence (Hematuria)

RARE  $\rightarrow$  [already on Anti-GBM disease  
Immunosuppression] (Ab against  $\alpha_5$  subunit).

## POLYCYSTIC KIDNEY DISEASE

Group of inherited Disorders characterised by <sup>285</sup>

A) multiple cysts in multiple organs

Kidney

Liver

Pancreas

Spleen

B) Berry Aneurysm

↑ risk of SAH

C) Colonic Diverticuloses

↓

Recurrent Colitis.

↓

↑ oxalate reabsorp" from gut

↓

Hyperoxaluria

↓

Oxalate Renal calculi

Mode of  
Inheritance

AD - PKD MIC

AR - PKD Rare

↓

Never survive > 10 yrs  
of age

↓

survive till adulthood

Called - adult - Polycystic KD

APKD-1

APKD-2

PKHD (Hepatic)

POLYCYSTIN - 1

POLYCYSTIN - 2

Fibrocystin

Chromosome 16

Chromosome 4

Chromosome 6

moderate form

mild form

most severe

20-30 yrs.

30-50 yrs of age

I.U. Life / Infancy

c/f

AD

Recurrent Loin Pain <sup>M/c</sup>  
 + Hematuria / fever (Infection in  
 Renal cyst)

- M/c - extra-renal (Hepatic cyst)
- mechanical compression - Bl. radicles
- cholestasis/ Cholangitis

|             |                                |                                |
|-------------|--------------------------------|--------------------------------|
| <u>Asis</u> | USG < 30 yrs                   | 30-59 yrs                      |
| ⊕           | ≥ 2 renal cysts<br>each kidney | ≥ 4 renal cysts<br>≥ 2 in each |
|             | ≥ 1                            |                                |

Rx - Renal Transplant  
 No Recurrence  
 Good Prognosis

AR

- oligohydramnios (30% fetal loss)
- Uremic symptoms in infancy
- ESKD ≈ 10 yrs of age
- Cirrhosis ≤ 10 yrs of age  
 (CAROLI's Disease = Defect of Intra-Hepatic Biliary Radical)

Present ≈ 3% cases

No cure  
 grave prognosis

# RENAL REPLACEMENT THERAPY

287

BEST FORM → TRANSPLANT

- Potential cure
- Better survival
- Better quality of life

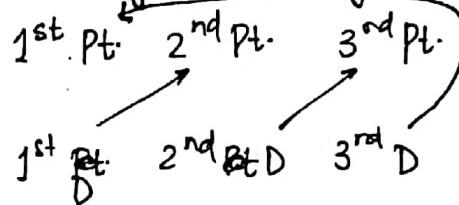
DIALYSIS

only filtration.  
Palliative Rx only

Limited Donor Availability

DOMINO Tx

Kidney swapping



HLA Registry

All Sx must be done on  
Same calendar  
(Limits - chain size)

HAPLO-Identical

(MHC / HLA matching) — 6 Ag matching

|          | A  | B  | C   |
|----------|----|----|-----|
| Class I  |    |    |     |
| Class II | DP | DQ | DR. |

> 3 = good match.

≤ 3 = Poor match.

(Less than half match)

- Most imp. HLA match is HLA-DR

↓  
Best success

## DIALYSIS

HEMODIALYSIS (H.D.)

Vascular access

(Cannula, AV fistula)

High Complications Rates

(Bleeding, sepsis, thrombosis)

H.D. center

(Limited availability)

Biocompatible - methyl  
cellulose polymers (filter)  
(High cost)

PERITONEAL (P.D.)

• Intraoperative catheter

placement → done ↓ LA

Low complication rates

(≤ 1% MRK → Peritonitis)

• no problem

only c/I → Part H/O recurrent  
GI Sx

Lower cost - omentum acts as  
filter

|                                                                                                                                                                                                                                                                                                                |                                                                                                                                                  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>• <u>Risk</u> → Infection transmission<br/>(HIV, HepB, HepC, CMV)</li> </ul>                                                                                                                                                                                            | <ul style="list-style-type: none"> <li>• NO Risk → Installing sterile peritoneal Dialysate fluid</li> </ul>                                      |
| <ul style="list-style-type: none"> <li>• Huge Hemodynamic/osmotic shift → poorly tolerated</li> <li>(M/c) acute comp' → <u>HYPOTENSION</u> <ul style="list-style-type: none"> <li>- Muscle cramps / Fatigue</li> </ul> </li> <li>• Sudden cardiac death<br/>In cardiomyopathy EF &lt; 15%<br/>↳ C/I</li> </ul> | <ul style="list-style-type: none"> <li>• Low shifts → Better Tolerated</li> </ul> <p>Safe in cardiomyopathy<br/>* Post cardiac Sx</p>            |
| <ul style="list-style-type: none"> <li>• Risk → HYPOGLYCEMIA</li> </ul> <p>Preferred form.<br/>Excellent filtration Rate<br/>800 - 1200 mL/min</p>                                                                                                                                                             | <ul style="list-style-type: none"> <li>Risk → HYPERGLYCEMIA/<br/>wt. gain</li> </ul> <p>Poor filtration<br/>15 - 25 mL/min.<br/>Only Back-up</p> |

### DIALYSIS ASSOCIATED AMYLOIDOSIS

- Accumulation of  $\beta_2$  microglobulin ( $\beta_2$ -MG)
- In the musculoskeletal system
- M/C → Entrapment neuropathy
- On dialysis  $\approx$  3-7 yrs
- Neither form (HD/PD) can filter  $\beta_2$ -MG.
- X-Ray Hand- Deposits in metacarpals.
- only Rx = Renal Transplant

## PRE - TRANSPLANT - Indications

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- 1) APKD
- 2) Horse-shoe Kid
- 3) Obstructive uropathy

} ↑ Risk of infections in the native kidneys

↓  
Post Transplant  
Immunosuppression

Septicaemia → stop Immunosuppressants

↓  
Rejection of Graft



CNS

achin\_mehra9@yahoo.com

PP Prayag Achin ~~mehra~~ mehra



# SEIZURE DISORDER & EPILEPSY

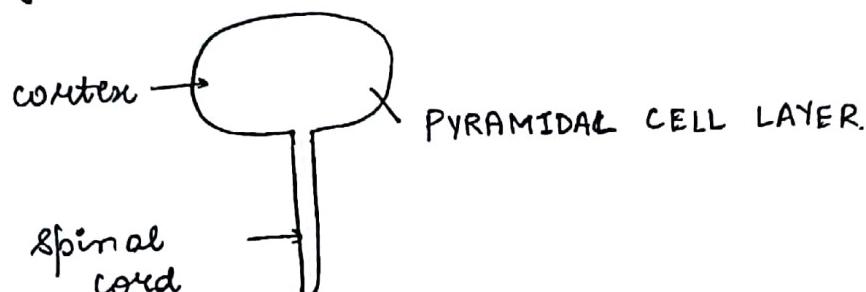
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## SACCIRE

= to take possession of

## SEIZURE

Polloxydral event due to hypersynchronous CNS discharges



## EPILEPSY

≥ 2 unprovoked seizures

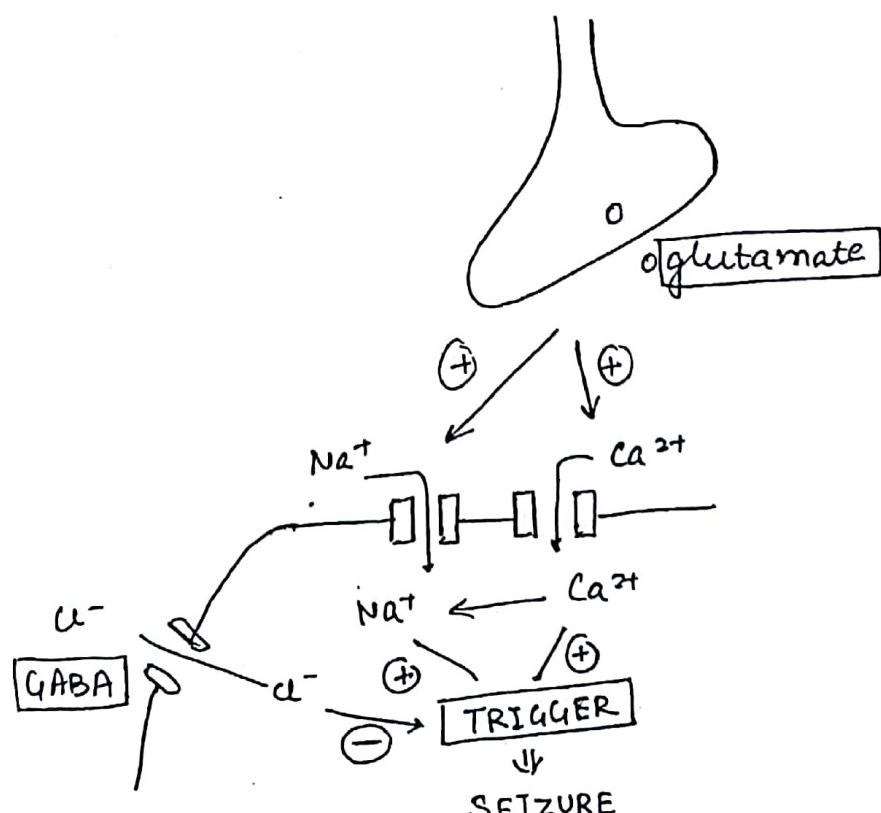
## EPILEPTOGENESIS

↑ GLUTAMATE

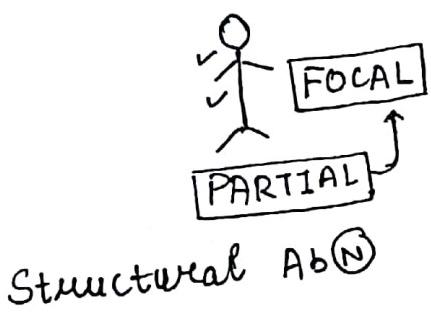
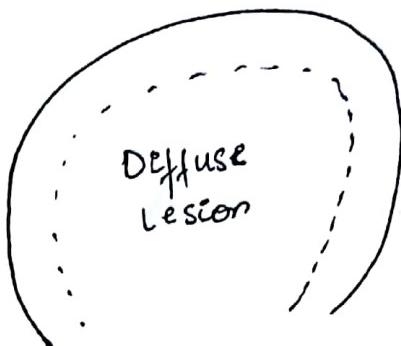
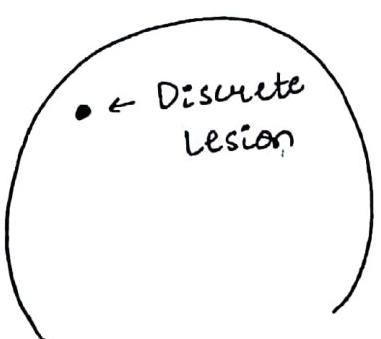
excitatory

↓ GABA

Inhibitory



## CLASSIFICATION OF SEIZURES



### DRUGS

Antibiotics - Quinolone

Antivirals - Acyclovir

Antimalarials → mefloquine  
chloroquine

Analgesics → Tramadol

### TOXINS

ABUSE

cocaine

Amphetamine

WITHDRAWAL

Alcohol

### METABOLIC

1)  $\downarrow \text{Na}^+$  (Mic Biochemical Ab(N) ppt.)  
 $\downarrow$  (seizure)

due to cerebral oedema  
 $<100$  ↑

2)  $\uparrow \text{K}^+$ ,  $\downarrow \text{K}^+$  → doesn't cause seizure.

## FOCAL SEIZURES

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### LOSS OF CONSCIOUSNESS

" Contact

" Cognition

→ (+) = Dys cognitive (complex) ←  
PARTIAL

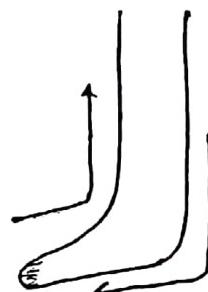
→ (-) = Non Dys cognitive (simple) ←

### TODD'S PALSY

- Post ictal Paralysis
- Self recoverable

↳ Starts in **1st 24 hours** of onset

### FOCAL SEIZURE



Distal → Proximal

### JACKSONIAN MARCH

→ focal seizure arising from in a Limb.

## GENERALISED

### ABSENCE SEIZURE / PETIT MAL EPILEPSY

### PYKNOLEPSY

- Loss of contact w/ environment
- Tone of Body (N)
- Abrupt onset
- ≤ 30 Sec
- Subtle Motor Signs (+)  
(minor)
- AURA (-)
- NO post ictal confusion

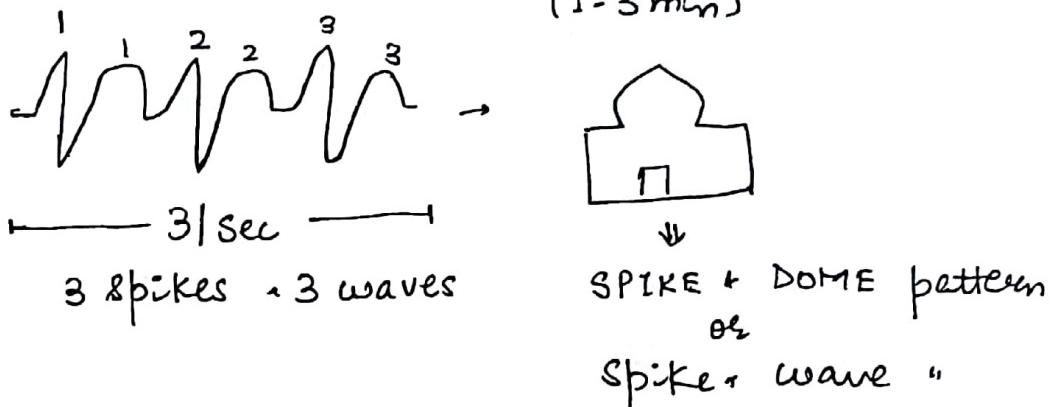
Starts - 4-8 yrs of age

Spontaneous Remission

in 60-70% by 18 years of Age

EEG :- BI/L 2-4 Hz spike + wave

Precipitated by Hyperventilation.  
(1-3 min)



### ATYPICAL ABSENCE SEIZURE

- Loss of consciousness - Less abrupt  
↑ Duration.
- mental Retardation
- Structural Abn
- EEG -  $\leq 2.5$  Hz spike + wave  
(slow)
- Resistant to Anti epileptic Drug

### MYOCLONIC SEIZURE

↓  
jerky movement

CAUSE - 1> Hypoxia

2> Degenerative

H/o Hanging → compresses Carotid  
↓  
cause hypoxia.

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~~000~~ JUVENILE MYOCLONIC EPILEPSY

- Early Adolescence
- Family H/o
- Chromosome No. 6
- unknown cause. ⇒ x hypoxia  
x Degeneration.

→ B/L Myoclonic jerks

- ↳ on awakening
- ↳ ppt. by

Fatigue  
Alcohol

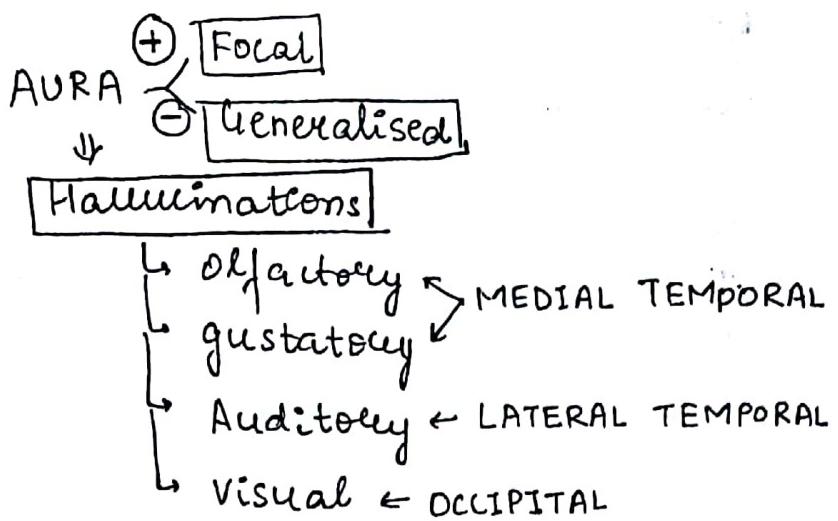
- IQ N
- Loss of consciousness ⊖
- subtle motor signs ⊖ → Eye blinking  
[AUTOMATISM] → Lip smacking

MAJORITY may turn into GTCS. pt

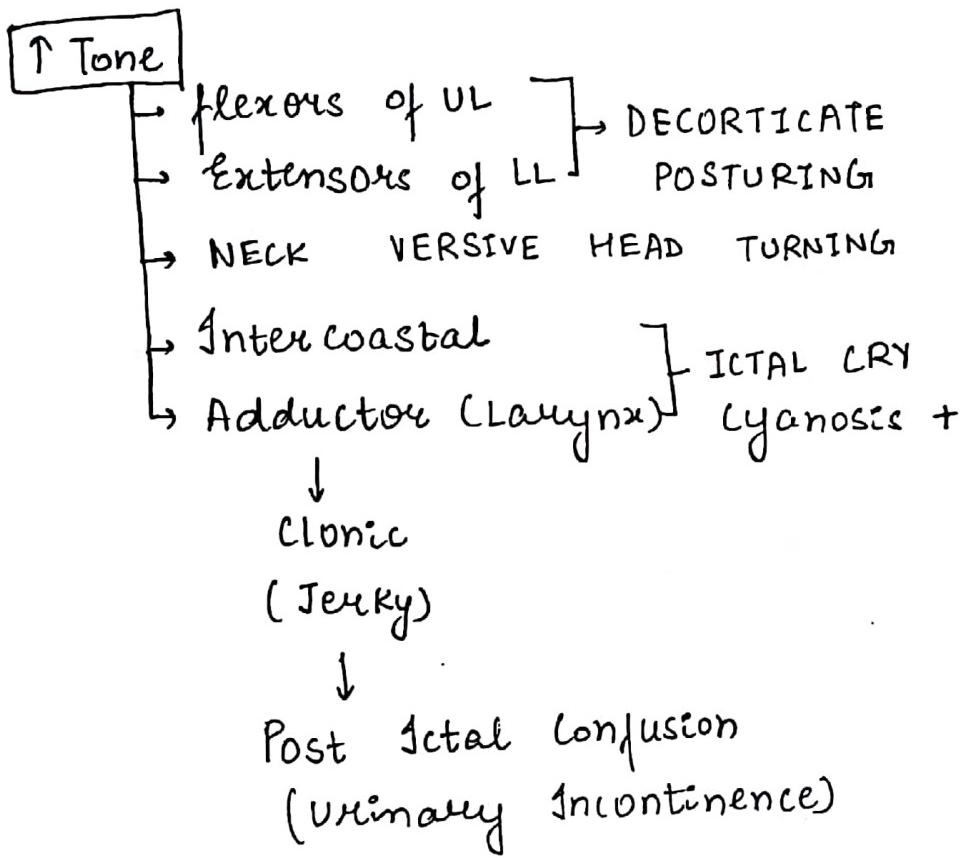
GENERALISED TONIC CLONIC SEIZURE  
GRAND MALL EPILEPSY

PREMONITORY SYMPTOMS -

Nausea  
vomiting  
Abdominal Pain



[NOTE: Aura seen in Focal Lesions.]



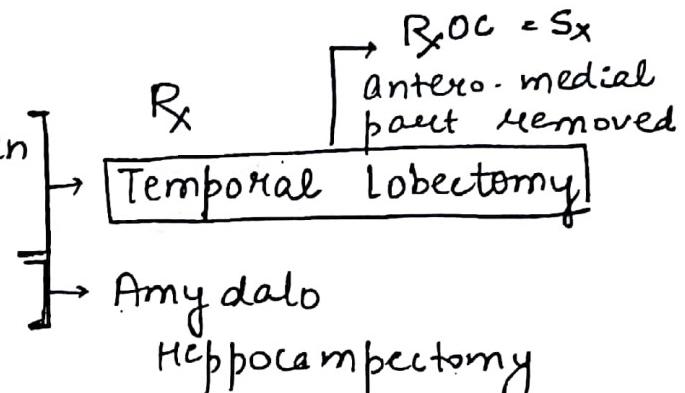
### JUVENILE MYOCLONIC EPILEPSY

- Myoclonus
- Majority → GTCS
- $\frac{1}{3}$ rd → Absence seizure

M/C presentation of JME is MYOCLONUS (AIZM<sub>299</sub>)

### MESIAL TEMPORAL LOBE EPILEPSY

- Focal seizure + Loss of Consciousness [DYSGONITIVE]
- DEJA VU
- Febrile seizure.
- Enlarged Temporal Horn  
Small Temporal Lobe  
Hippocampal Sclerosis
- Resistant to anti-epileptics



S. PROLACTIN  
↑ 30 mins after True Seizure

### ANTI-EPILEPTIC DRUG

A.E.D. X 2 years → TAPER → 3<sup>rd</sup> year  
↓  
Stop.

Sudden withdrawal of Drug ⇒ ppt. seizure.

Seizure ppt. while withdrawal in 1st 3 months more commonly.

|               |                        |               |
|---------------|------------------------|---------------|
| <u>X DRUG</u> | 1st episode of seizure | <u>✓ DRUG</u> |
| Provoked      |                        | Unprovoked    |

- Febrile seizure
- Alcohol withdrawal
- ↓  
BZD - Injectable

- Status epilepticus
- Family H/o (+)
- Abn neurological exam"

Chlordiazepoxide

Oral

for gen. alcohol. withdrawl  
not for seizures

Ab(N) EEG  
CT/MRI.

300

IOC

Seizure  $\Rightarrow$  EEG

DOC =

$\uparrow$  EFFECT

$\downarrow$  SIDE EFFECT

FOCAL

L - Lamotrigine  $\rightarrow$  STEVENS JOHNSON SYNDROME (1%)

O - Oxcarbamazepine  $\rightarrow$   $\downarrow$  Na<sup>+</sup> (SIADH)

C - Carbamazepine  $\rightarrow$  Aplastic anaemia

P - Phenytoin

L - Levetiracetam

irritability mood disorder

[6H]

hypersensitivity

hyperglycemia

hyperplasia of gums

hydantoin syndrome

irsutism

hepatitis

+ megaloblastic anaemia

[ $\uparrow$  excretion of folate]

+ osteomalacia

FETAL HYDANTOIN  $\rightarrow$

Microcephaly

Hypoxia of Limbs

Cleft  $\begin{cases} \text{Lip} \\ \text{Palate} \end{cases}$

Valproate

Phenytoin

Carbamazepine

## GTCS

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Valproate  
Lamotrigine  
Topiramate

## ABSCENCE

ETHOSUXIMIDE - DOC

Valproate ←  
Lamotrigine

## ATYPICAL ABSENCE SEIZURE

000



## SAFEST A.E.D

Lamotrigine > Carbamazepine > Pheno barbitone  
↓ teratogenicity  
↑ sedative even for fetus

**DOC** → as per seizure type  
monotherapy  
Lowest effective Dose

GTCS → Valproate → Neural Tube →  $\text{N.Preg.} = 1-2\%$ .  
Defect  
 $\bar{c} \text{ A.E.D.} = 10-20\%$ .

A.E.D is not 100% Teratogenic

Do not change Rx During ♀ becoz changing  
Rx can ppt. seizure [Break Through].

Seizure frequency during ♀

50% - Unchanged

20% - ↓

30% - ↑

→ emesis,

Y ↑ in 30%

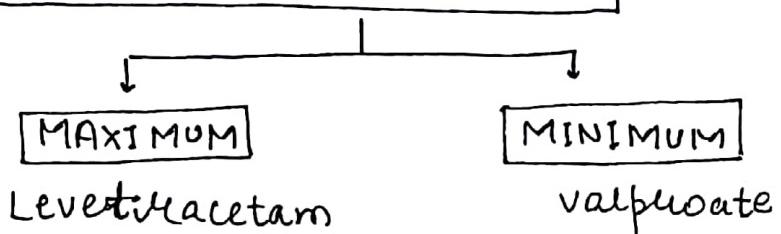
302

- 1) Lemesis → Labour of drug
  - 2) Hormones

Progesterone  
↑ Seizure  
threshold

Estrogen [epileptogenesis]  
1 seizure  
threshold

## A.E.D. Excreted In Breast Milk



Breast feeding is recommended

AED is also continued

JME

A·E·D. x Lifelong

DOC = Valproate

## Levetriacetam

⇒ DRUGS NOT USED IN JME

→ Carbamazepine

→ Phenytoin

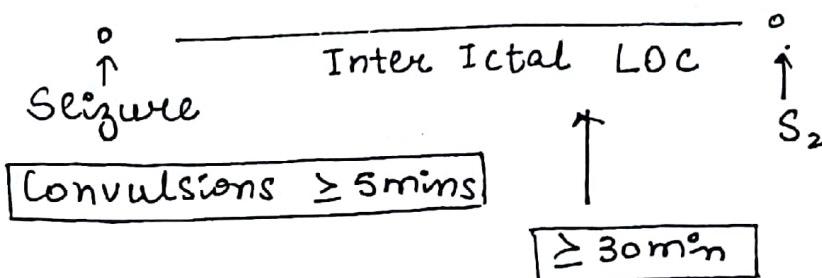
→ Lamotrigine

→ ↑ myoclonus

⇒ PRE ♀ on valproate  
↓ change to  
Levetiracetam

## STATUS EPILEPTICUS

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### EPILEPSIA PARTIALIS CONTINUA

- Continuous partial seizure
- ⇒ Status epilepticus in focal seizure

1st Drug

LORAZEPAM or MIDAZOLAM  
(0.1 mg/kg)  $\frac{\text{Dose}}{\text{Dose}}$  (0.2 mg/kg)

I.V. A.E.D.

PHENYTOIN

20mg/kg  $\downarrow$  Order kinetics @ 50mg/min  $\downarrow$  cardiotoxic

$\times$  Dextrose  $\Rightarrow$  Phenytin ppts  
Normal Saline  $\equiv$  dextrose

Pos PHENYTOIN  
@ 150mg/min

$\downarrow$  Hypersensitive  
mixed  $\equiv$  Dextrose  
I/M

VALPROATE  
(25mg/kg)

OR

LEVETRIACETAM  
(20-30 mg/kg)

[POST - TRAUMATIC EPILEPSY  $\rightarrow$  LEVE TRIACE TAM.]

$\downarrow$  + Seizure

I.V. MIDAZOLAM

$0.2 \text{ mg/kg} \rightarrow 0.2 - 0.6 \text{ mg/kg/h}$

OR

I.V. PROPOFOL

$| + \text{Seizure}$



## THIOPENTONE

CARBAMAZEPINE → not recommended in status  
as found in oral form

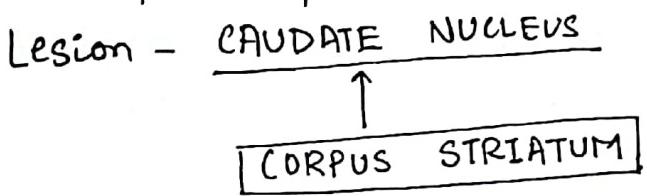
### MOVEMENT DISORDERS

#### ATHETOSIS / CRAWLING

- Slow
- Sinus
- Wriggling
- Seen in Lesions of GLOBUS PALLIDUS → G A P

#### CHOREA / DANCE like movement

Semi purposeful movement



#### CAUSES -

- C - Chorea Gravidarum
- H - Huntington's Chorea
- O - OCP
- R - Rheumatic / Sydenham's Chorea
- E - Endocrine / Thyrotoxicosis.
- A - Atherosclerotic / Senile
- M/c/c ⇒ **SLE**

## HEMIBALLISMUS

⇒ Exclusively on ONE SIDE

305

- ✓ Large Amplitude
  - ✓ Flinging
  - ✓ Proximal
  - ✓ Limb
  - ✓ Lesion ⇒ SUBTHALAMIC NUCLEUS (STN)
- ↓  
C/L

## PARKINSONISM

Degeneration / Atrophy ⇒ SUBSTANTIA NIGRA  
PARS COMPACTA (SNpc)

### LEWY BODY

- Intra-neuronal
- Intra-cytoplasmic
- Eosinophilic inclusion body
- Contains α-synuclein

↓ DA

↑ ACh

Level  $\frac{N}{100\%} \rightarrow 70\%$   
 $\downarrow 30\%$

TREMORS

RIGIDITY

### ETIOLOGY :-

1) DRUGS ⇒ DA ⊥  
(H/c/c of  
2° Parkinsonism)

### TYPICAL ANTIPSYCHOTICS

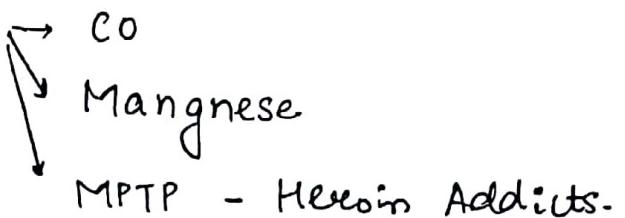
Haloperidol

CPZ

METOCLOPRAMIDE

DA Depleters ⇒ Methyldopa  
Reserpine

## 2> TOXINS



306

## 3> TRAUMA

BOXERS

## 4> FAMILIAL / GENETIC

MUTATIONS

GENES → α-synuclein gene

PARKIN gene

Chromosome 4

LRRK-2 gene

Chromosome 12

Chromosome 4

( $<40$  yrs       $>40$  yrs)

Age of onset

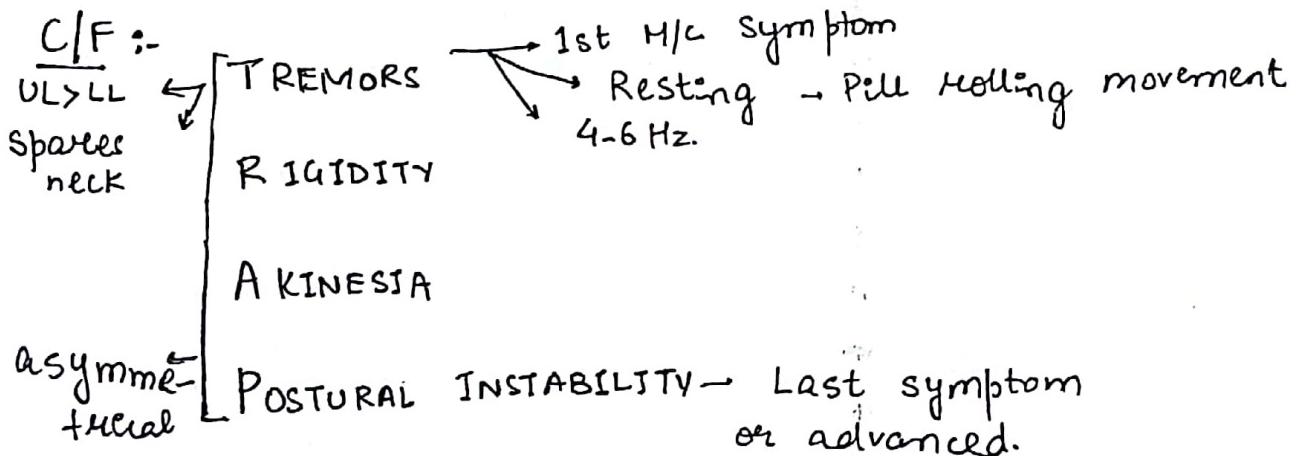
EARLY ONSET

## 5> IDIOPATHIC -

85-90% pts.

PARKINSON DISEASE. (M/C type)

" PARALYSIS AGITANS



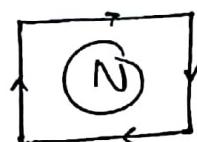
TITUBATION → ⊖ Parkinsonism  
↓ ⊕  
cerebellum

307

## TREMOR

RESTING TREMOR ⇒ PARKINSONISM

INTENTIONAL TREMOR ⇒ CEREBELLAR LESIONS



FLAPPING TREMOR = HEPATIC ENCEPHALOPATHY  
"ASTERIXIS" UREMIC "  
 $\text{CO}_2$  narcosis

FINE TREMORS = THYROTOXICOSIS

### BENIGN ESSENTIAL TREMORS

- 5 - 11 Hz
- AD inheritance
- UL > LL
- ORIGIN = cerebellum
- ↑ anxiety
- ↓ on alcohol consumption
- = Rx → Propranolol



RIGIDITY - BEST Jt to show Rigidity = WRIST  
Resistance to passive movement

LEAD PIPE → EXTRA PYRAMIDAL SYNDROME

superimposed tremors on COG WHEEL → PARKINSONISM

UL = COG WHEEL

LL = LED PIPE

zigzag lead pipe CLASP KNIFE - UMNL

## RIGIDITY

Tone ↑ Flexors = Extensors  
Bidirectional

## SPASTICITY

308

Flexors > Extensors  
unidirectional  
velocity dependent

## GAIT

FESTINATING GAIT → Parkinsonism  
(ready to run)

Kinesia Paradox

↳ ↑ acceleration on running

+ spasticity  
↑ extensor tone  
wk. Distal Proximal  
↑

CIRCUMDUCTION GAIT - Hemiparesis → corticospinal tract

WADDLING GAIT → Myopathy (Proximal)

Lurching GAIT - Polio Lesion → Ant. Horn cells.

BROAD BASED - Cerebellum → Drunken Gait

HIGH STEPPAGE - Foot Drop] neuropathy  
Deep Peroneal N/V

STAMPING → TABES DORSALIS

↳ lesion → post column

loss of vibration

## POSTURAL INSTABILITY

Loss of Postural Reflexes → FALL

### MICROGRAPHIA

small handwriting

(N) I am a doctor

(PD) I am a dent-

MONOTONOUS SPEECH

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Hypoacusis

MASK LIKE FACE

Depression

Dementia

PARKINSONISM + ATYPICAL PK

SYMMETRICAL  
unresponsive to  
Levodopa

1> Progressive Supranuclear Palsy / STEEL RICHARDSON SYNDROME

- Extended Posture
- Defective downward gaze
- H/o fall ↙ early in this type
- Dementia
- ② Tremors

2> LEWY BODY DEMENTIA (LBD)

Parkinsonism + visual Hallucination

3> MULTIPLE SYSTEM ATROPHY (MSA)

Parkinsonism + cerebellum + Autonomic symptom Instability

4> CORTICO BASILAR DEGENERATION (CBD)

Parkinsonism + myoclonus + Dystonia  
sustained Posturing

RX

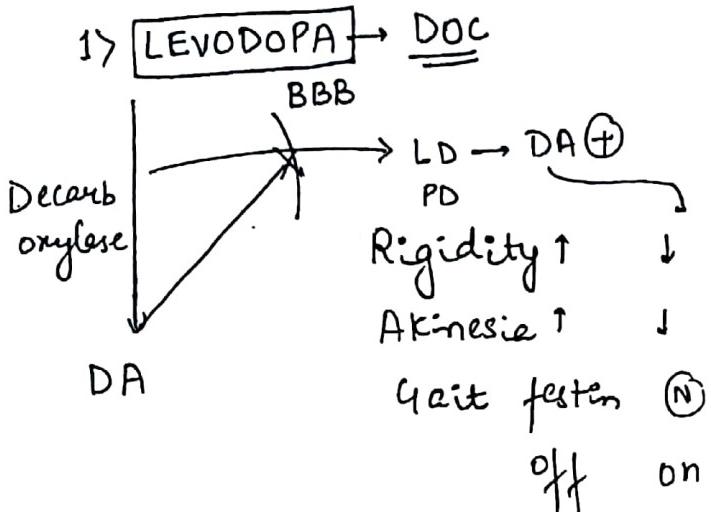
310

↓ DA  
(rigidity)

PD

T Ach

(Tremor)



2) ANTIACHOLINERGICS

TRIHEXYPHENYDYL

2) PERIPHERAL DECARBOXYLASE

INHIBITORS

- CARBIDOPA
- BENZERAZIDE

3) MAO B ⊖

- SELEGILINE
- RESAQUILINE  
(neuroprotector)

3) COMT ⊖

- ENTACAPONE
- TOLCAPONE

5) AMANTADINE

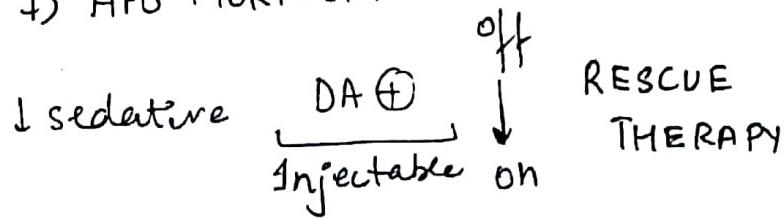
↑ DA Level

6) DA + D<sub>2</sub>

- PRAMIPRAZOLE
- Robinivore
- Rotigotine

7) APO MORPHINE

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## CEREBROVASCULAR ACCIDENT (CVA) STROKE

→ Focal neurological Deficit due to vascular cause  $> 24$  hrs

→ TIA (Transient Ischaemic Attack) -

$< 24$  hrs

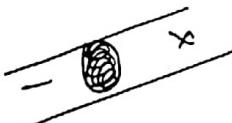
most  $\rightarrow$  for 1 hour

20 mL / 100gm brain tissue / min = Ischaemia +  
Infarction  $\ominus$

16 mL / min  $\times$  1 hour = Infarction  $\oplus$

0 mL / min  $\times$  4-10 min = DEATH

### CLASSIFICATION



ISCHEMIC (85%)

EMBOLIC (75%)

THROMBOTIC (25%)

H/c/c

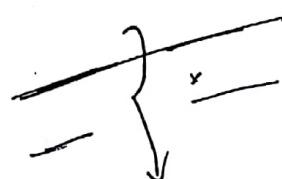
AF.

non-rheumatic  
AF

Most epileptogenic stroke

Embolic  $>$  H/c/g  $>$  Thrombotic

$\downarrow$   
cerebral oedema



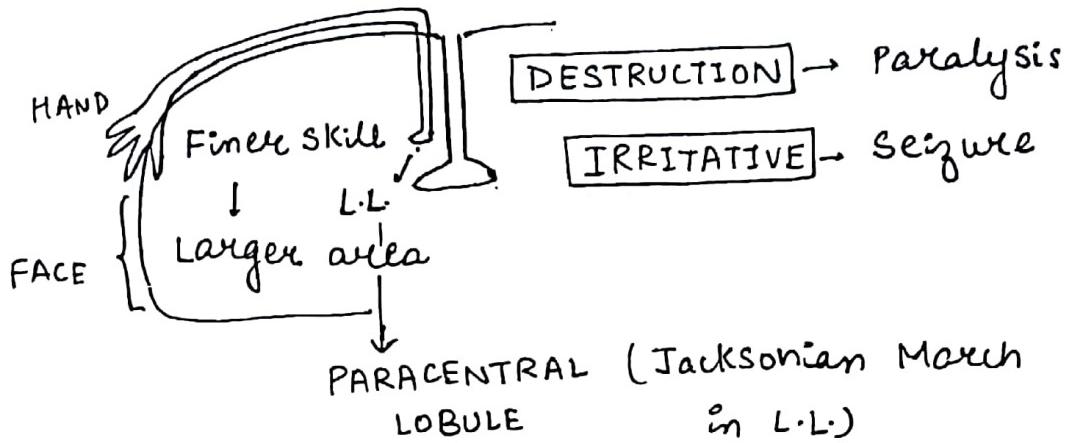
HAEMORRHAGIC (15%)

Lacunar Infarcts - sub cortical  
so no seizures

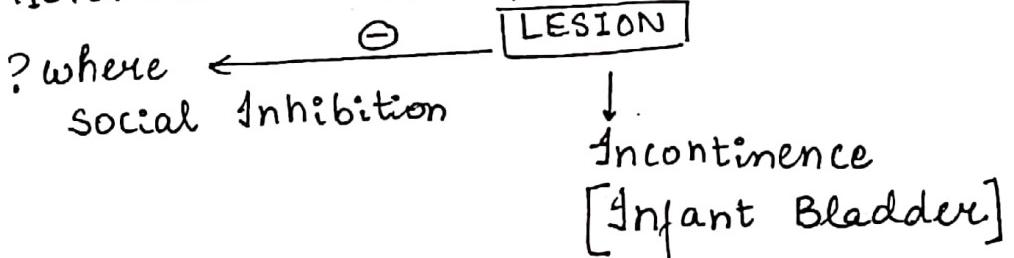
312

## FRONTAL LOBE

1) 1<sup>o</sup> MOTOR AREA

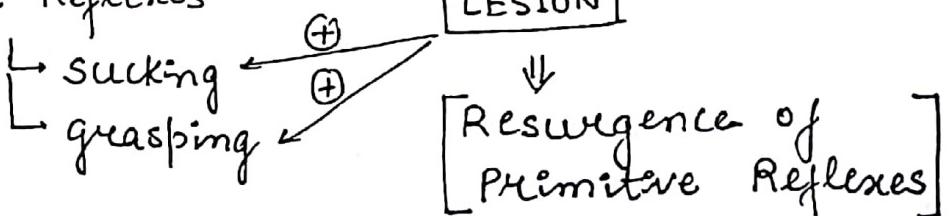


2) MICTURITION AREA



3) SUPPLEMENTARY MOTOR AREA

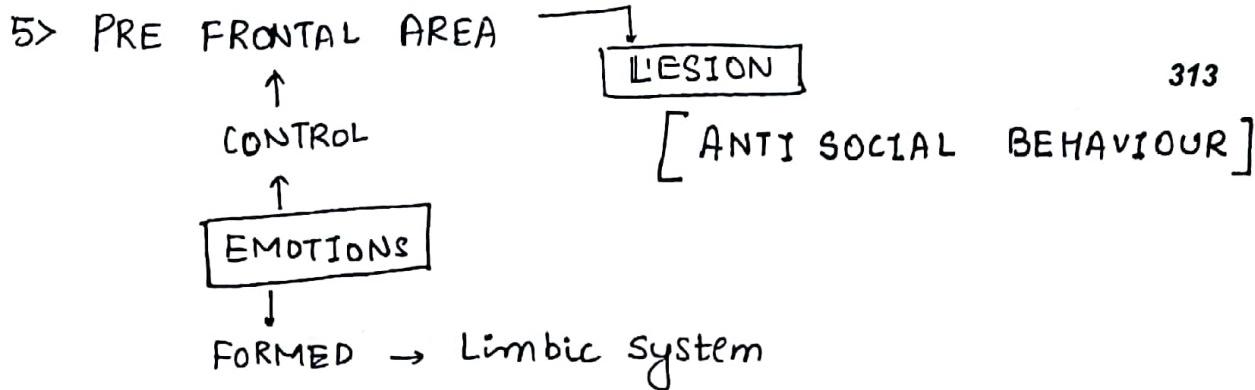
② Primitive Reflexes



4) BROCA'S AREA

→ word area

→ Located in Inf. Temporal Gyrus

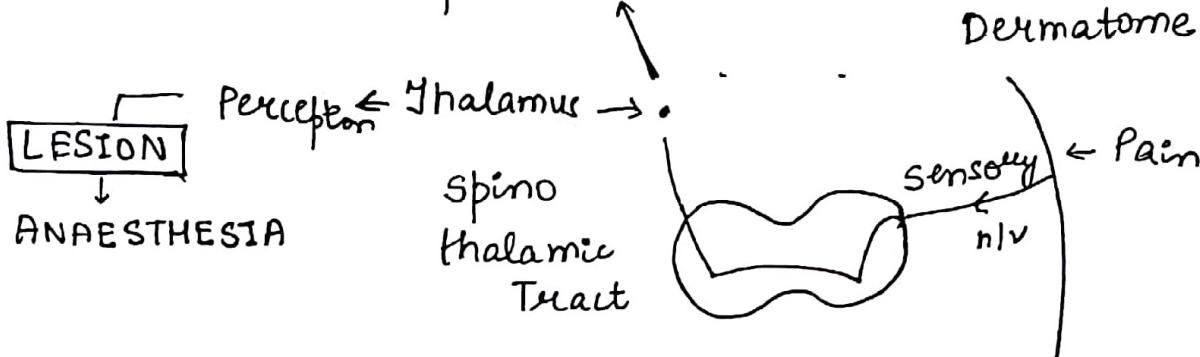


CIVIC LOBE = FRONTAL LOBE

### PARIETAL LOBE

1> 1<sup>o</sup> SENSORY AREA

Localisation of stimulus



2> STEREOGNOSIS

Ability to identify on touch.

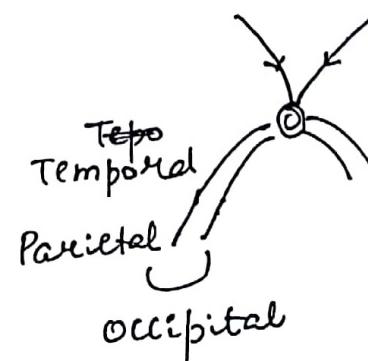
3> TASTE

LESION → DYSGUSIA

4> OPTIC RADIATION



SCOTOMA



## 5) ANGULAR GYRUS

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Stores images a/c

LESION

→ Reading

DEVELOPMENTAL

→ Calculation

a) R to L confusion

→ Naming Fingers

b) DYSGRAPHIA (Reading)

c) DYSLEXIA (Learning)

d) ACALCULIA

e) Finger AGNOSIA

cannot identify

## (N) BOMBAY

B O M B A Y

-

② to ① confusion

GERSTMANN SYNDROME

↓  
Lesion = L Hemisphere

## TEMPORAL LOBE

1) 1<sup>o</sup> AUDITORY AREA

Hearing ↓

LESION → CORTICAL DEAFNESS

2) WERNICKE's AREA

Sup. Temporal Gyrus  
Comprehension

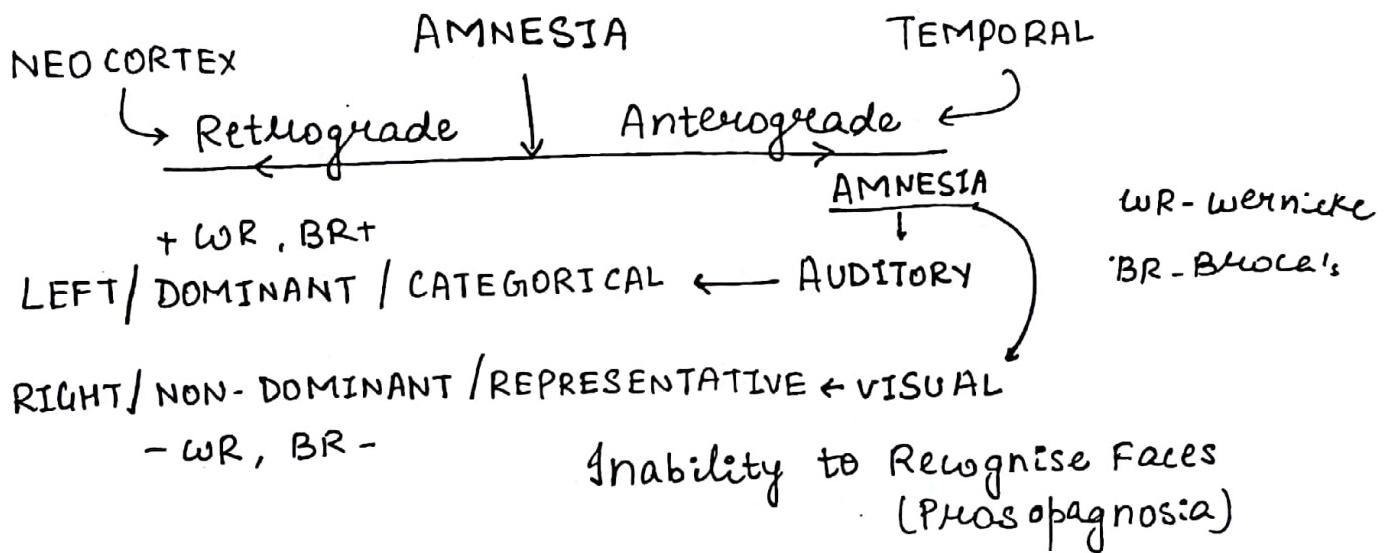
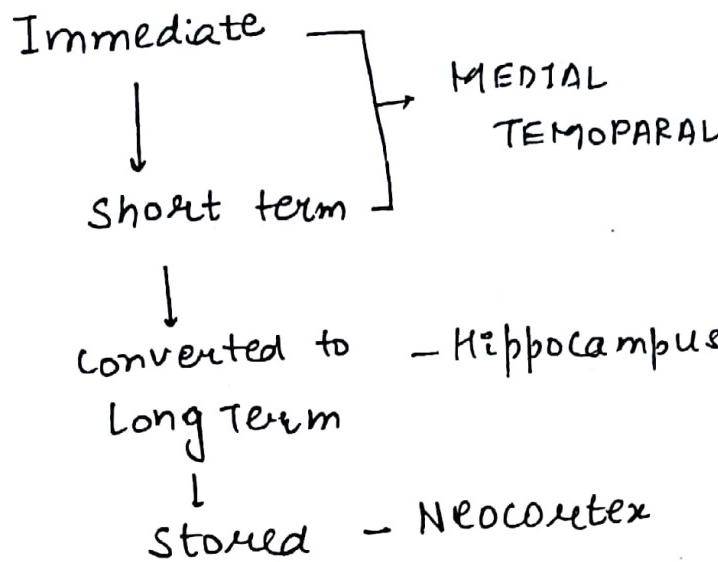
3) OLFACTION → ANOSMIA

4) OPTIC RADIATION → SCOTOMA

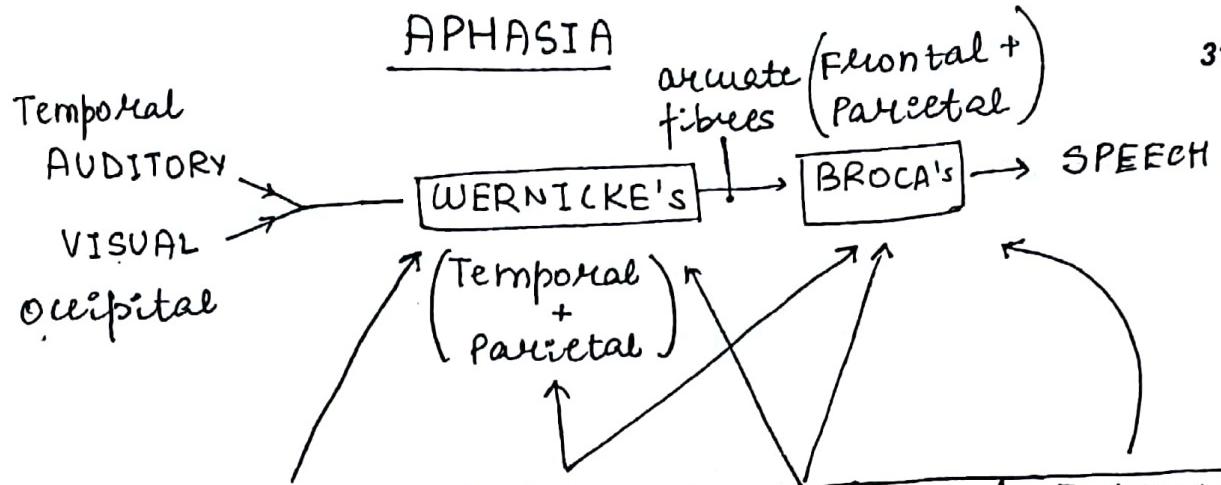
5) DEEP / MEDIAL TEMPORAL LOBE  
Memory

## MEMORY

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Handedness → Right → 90% ]  
                   ↓  
                   Left → 60% ]  
                   Left hemisphere  
                   ↓  
                   Dominant



| APHASIA                                             | COMPR. | NAMING                                                  | REPETITION | FLUENCY                               |
|-----------------------------------------------------|--------|---------------------------------------------------------|------------|---------------------------------------|
| WR.                                                 | (-)    | (-) Neologism                                           | (-)        | (N) / ↑<br>EXPLOSIVE<br>JARGON speech |
| BROCA                                               | (N)    | (-) Telegraphic speech<br>Melodic Circumlocution speech | (-)        | ↓<br>Insight (+)<br>Depression        |
| CONDUCTION<br>arcuate fibres damaged                | (N)    | (-)                                                     | (-)        | (N)                                   |
| TRANS CORTICAL<br>Sensory (Post)                    | (-)    | (-)                                                     | (N)        | (N) / ↑                               |
| TRANS<br>cortical<br>Sensory<br>Motor<br>(Anterior) | (N)    | (-)                                                     | (N)        | ↓                                     |

|                                                      |              |     |                  |     |
|------------------------------------------------------|--------------|-----|------------------|-----|
| Mixed<br>Trans<br>cortical<br>(Isolation<br>aphasia) | (-)          | (-) | (N)<br>Echolalia | (-) |
| Pure<br>Word<br>Deafness<br>Auditory<br>damage       | (-)          | (N) | (-)              | (N) |
| Pure<br>word<br>Blindness<br>(Alexia)                | ↓<br>Reading | (N) | (N)              | (N) |
| Anomic<br>Aphasia                                    | (N)          | (-) | (N)              | (N) |

MC type  
angular gyrus

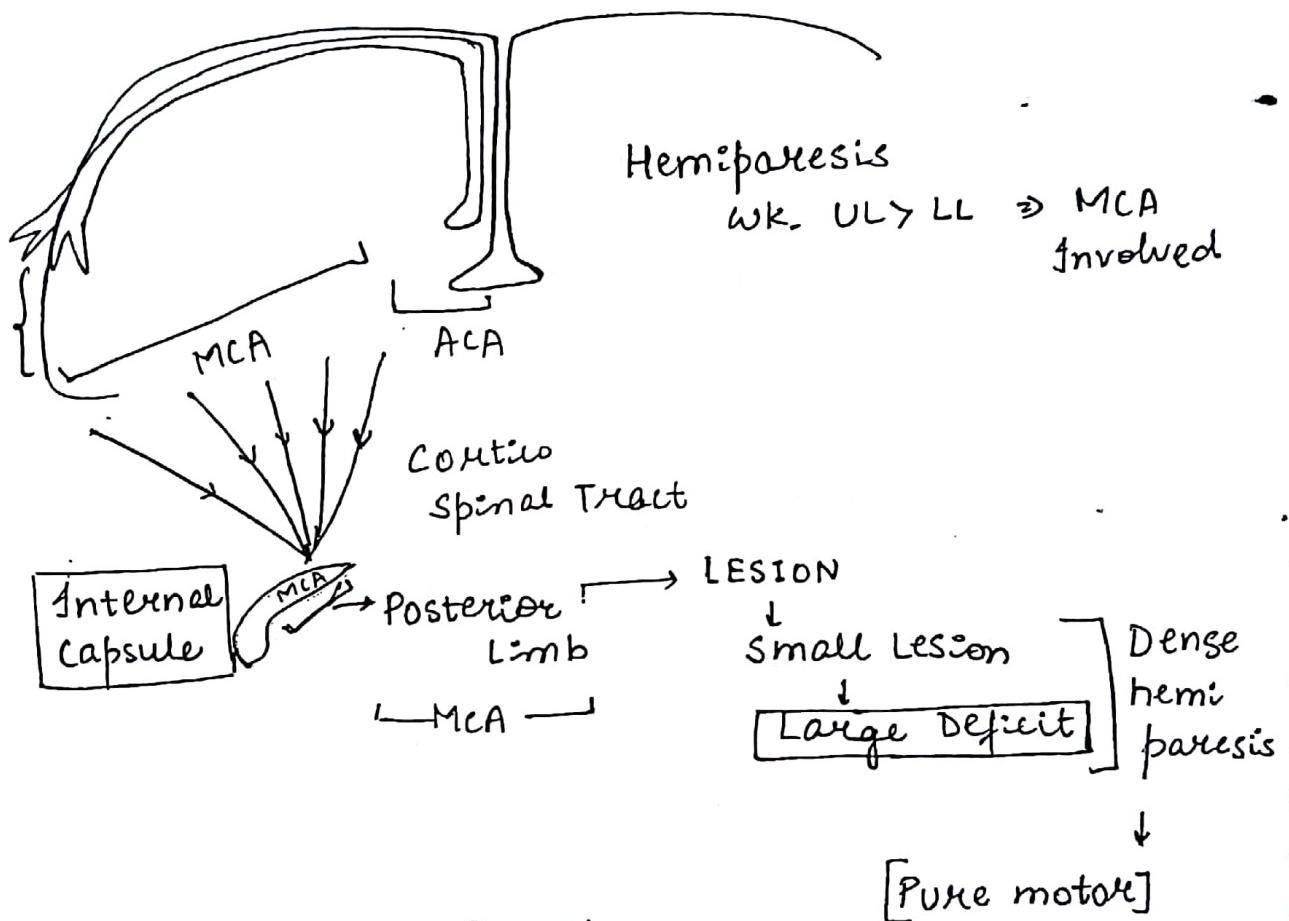
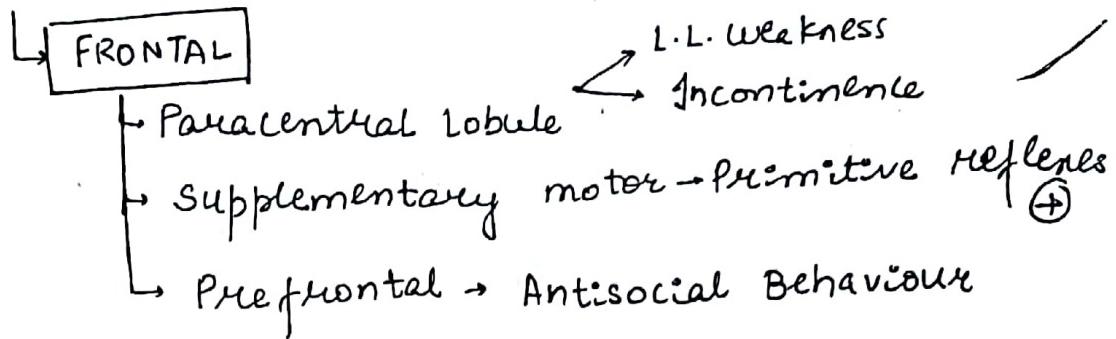
seen in  
 Alzheimer  
 Head Trauma  
 Metabolic  
 Encephalopathy

SCANNING speech      I AM A DOCTOR  
 ↳ CEREBELLAR Lesion.

⇒ Broca's Lesion ⇒ Couldn't write a dictation

## Ant Cerebral Artery

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APHASIA  $\rightarrow$  MCA (L)  $\rightarrow$  Broca's, Wernicke's

AMNESIA  $\rightarrow$  Post. cerebellar  $\rightarrow$  medial temporal artery  $\rightarrow$  Hippocampus

GAIT APRAXIA  $\rightarrow$  Ant. cerebral artery  
↳ Ⓛ movement

## Rx [ISCHEMIC]

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### 1> THROMBOLYSIS

Recombinant tissue Plasminogen activator (rtPA)  
(I.V.) = 0.9 mg/kg  
MAX DOSE = 90mkg  
10% → Loading Dose  
90% → Infusion × 1 hour.

WINDOW PERIOD = 4.5 hours  
from onset

### 2> ANTIPLATELETS

ASPIRIN

NO clopidogrel

### 3> ANTI COAGULANTS

HEPARIN

AF  
prosthetic valve

↓  
WARFARIN

| B                   | <u>POWER</u>              |
|---------------------|---------------------------|
| GRADING (MRC scale) |                           |
| 0                   | → no movement             |
| 1                   | → flickering              |
| 2                   | → with gravity eliminated |
| 3                   | → against gravity         |
| 4                   | → against Resistance      |
| 5                   | → NORMAL                  |

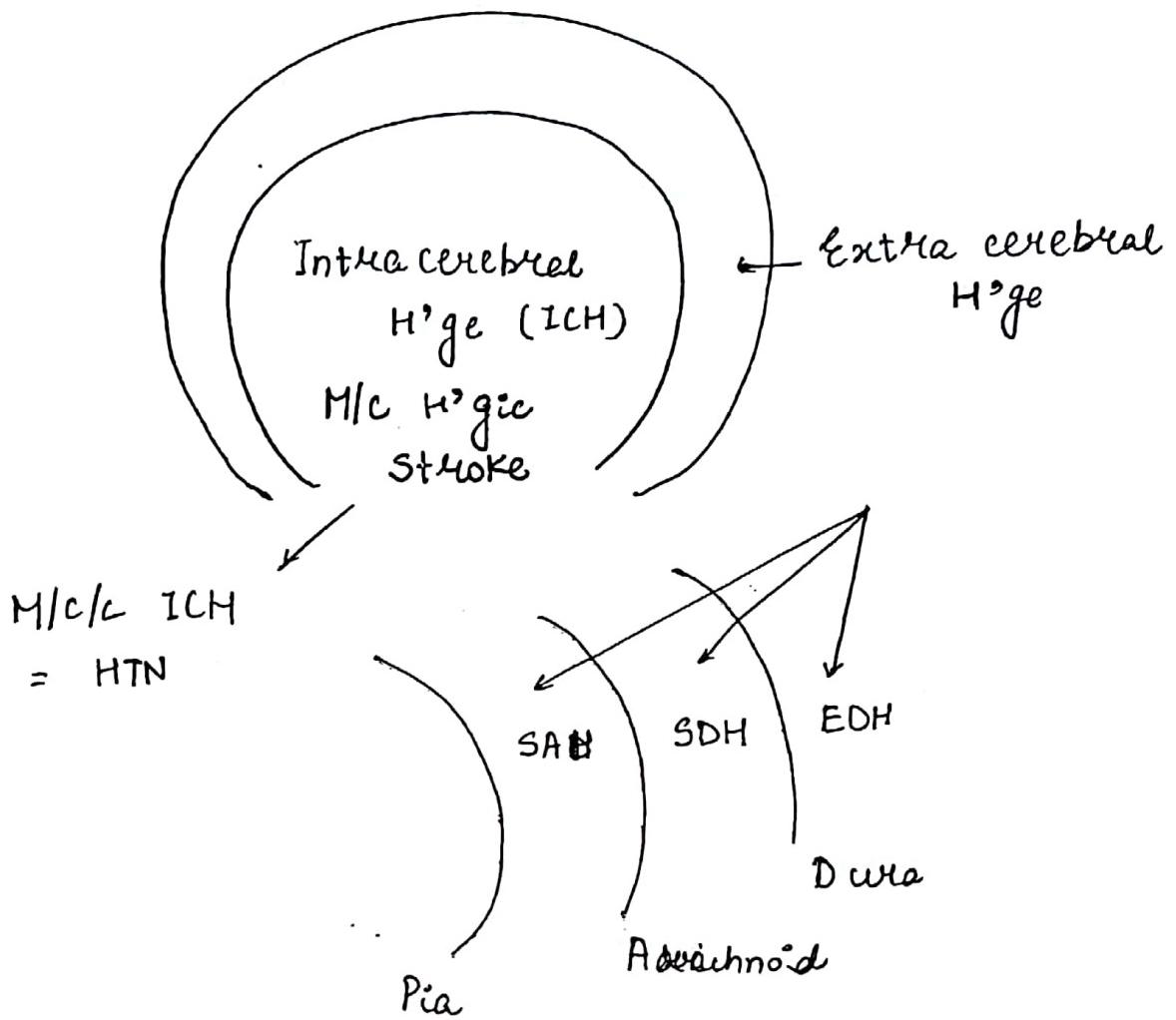
Power

↑ (1/5 → 4/5) → EMBOLIC

↓ (4/5 → 1/5) → THROMBOTIC

# HAEMORRHAGIC STROKE

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## HTN ICH

### SITES

1) Basal Ganglia (Putamen) ] M/c site HEMI PARESIS

2) Thalamus ← HEMI ANAESTHESIA

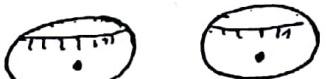
3) Cerebellum ← ATAXIA  
↓ VERTIGO ] Rx Decompression diameter > 3cm

Worst

Prognostic Pontine

B/L extensor Plantar

↑ HR  
RR  
Temp  
Sweating

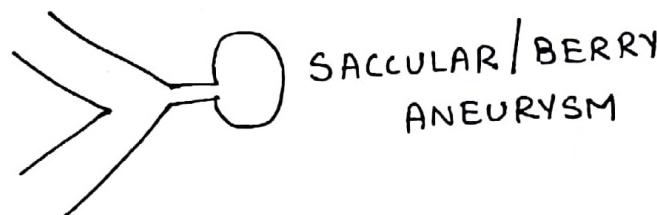
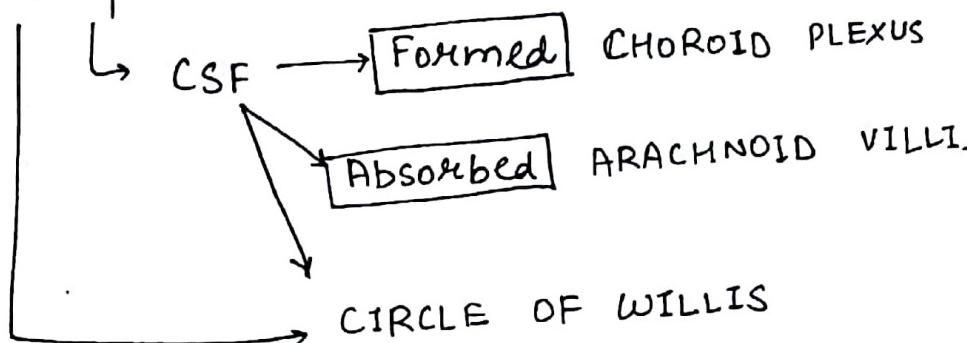


PIN POINT  
PUPIL

\* also seen in -

OP Poisoning  
→ morphine

S.A. Space



### ETIOLOGY

1> Trauma (M/c/c) (non-traumatic)

2> Rupture of Berry Aneurysm (M/c/c spontaneous SAH)

3> A-v malformations

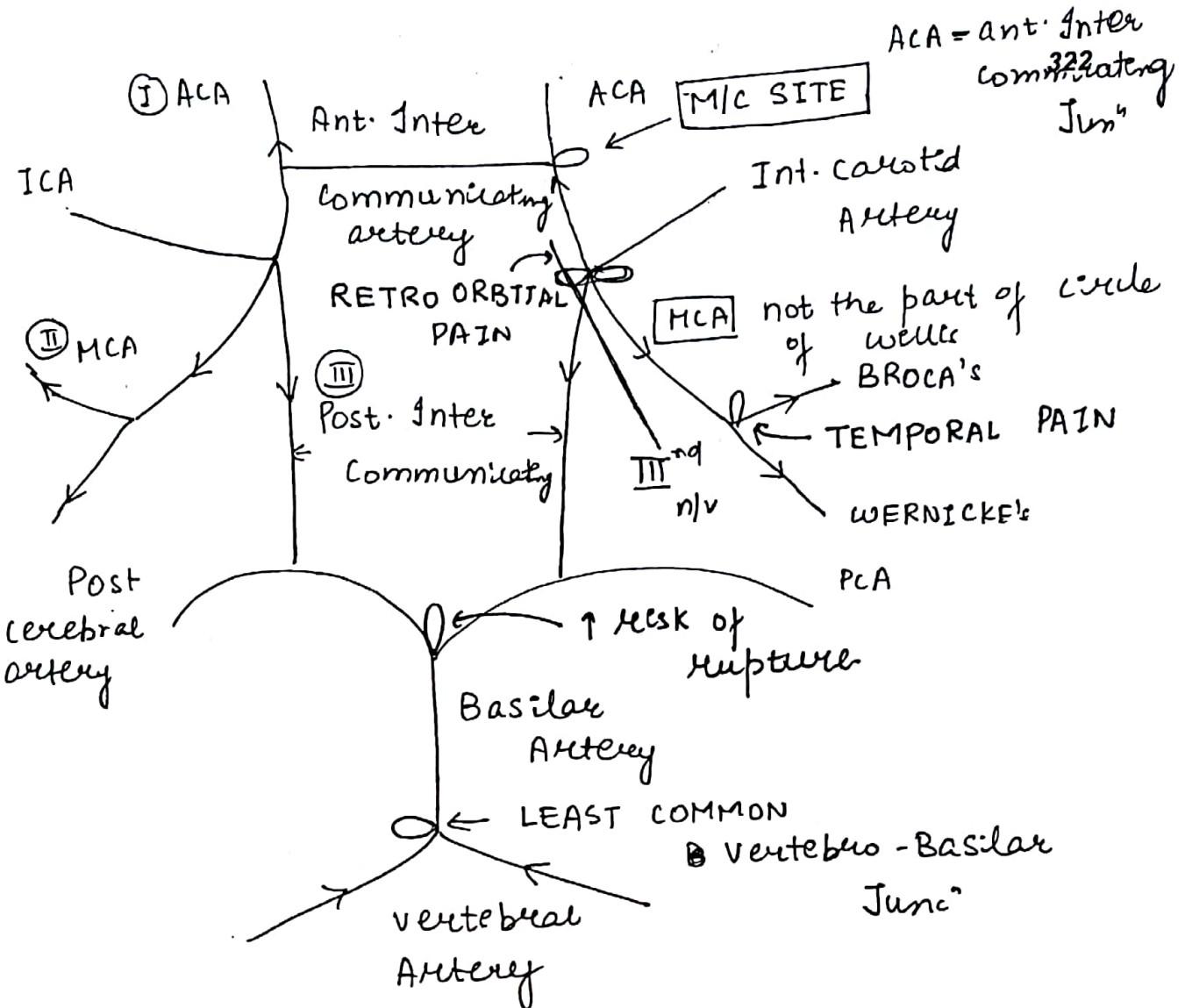
4> Extension from ICH

5> **Idiopathic**

→ LOCATION = Perimesencephalic cistern

→ Angiography → N

→ Source = venous



85% of aneurysm  $\Rightarrow$  ANT. CIRCULATION

15% of "  $\Rightarrow$  POST. CIRCULATION

Less common

$\uparrow$  Risk of Rupture

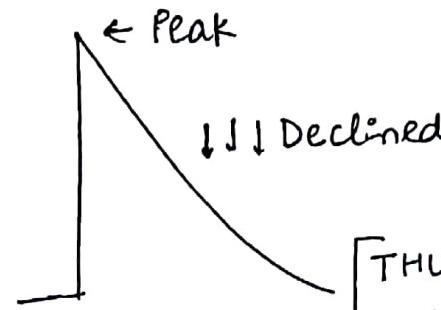
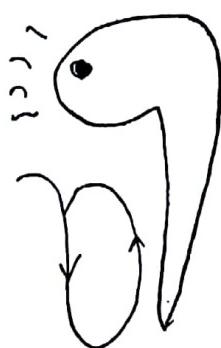
### M/c cranial n/v

- |                |               |                   |
|----------------|---------------|-------------------|
| Berry Aneurysm | $\Rightarrow$ | III <sup>rd</sup> |
| $\uparrow$ ICH | $\Rightarrow$ | VI <sup>th</sup>  |
| GBS            | $\Rightarrow$ | VII <sup>th</sup> |
| DM             | $\Rightarrow$ | III <sup>rd</sup> |
| HIV            | $\Rightarrow$ | VII <sup>th</sup> |
| Sarcoidosis    | $\Rightarrow$ | VII <sup>th</sup> |
- Paralyzed = VII<sup>th</sup>

C/F-

Onset / Immediate

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[THUNDER CLAP]  
HEADACHE

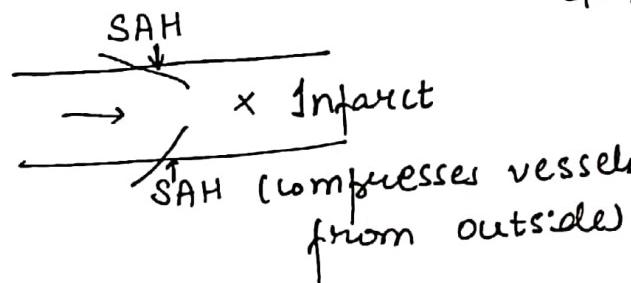
Neck Rigidity

Loss of consciousness (transient)

No focal neurological  
Deficit

DELAYED

1) **Vasospasm**

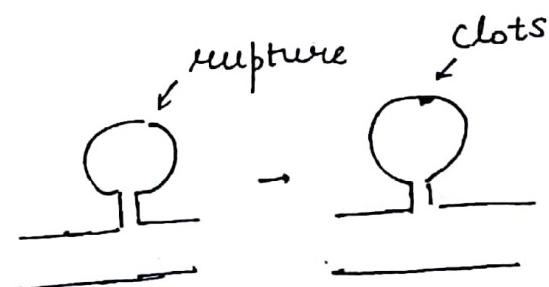
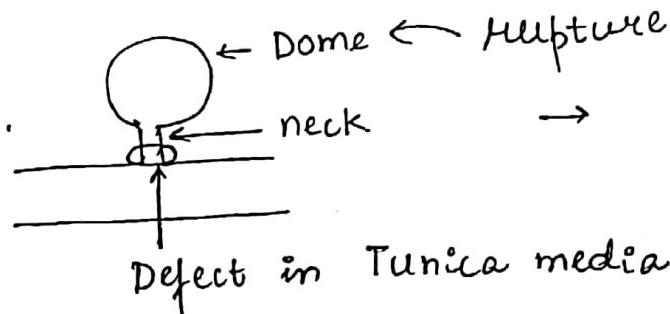


4-14 days after SAH

↑  
Peaks in 1st 7 days  
of onset

M.c.c → mortality  
morbidity

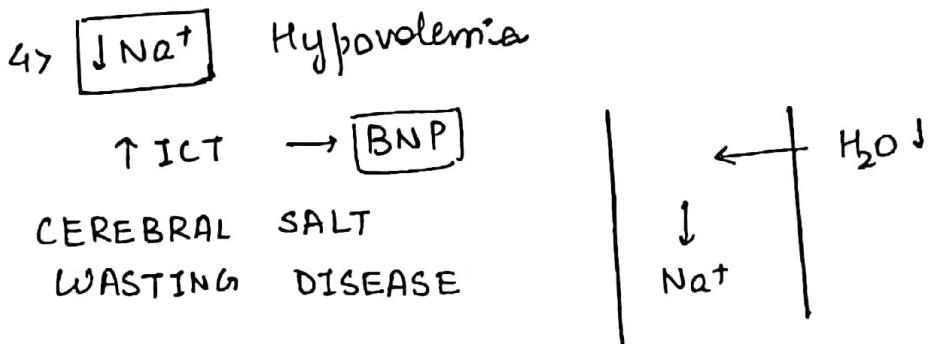
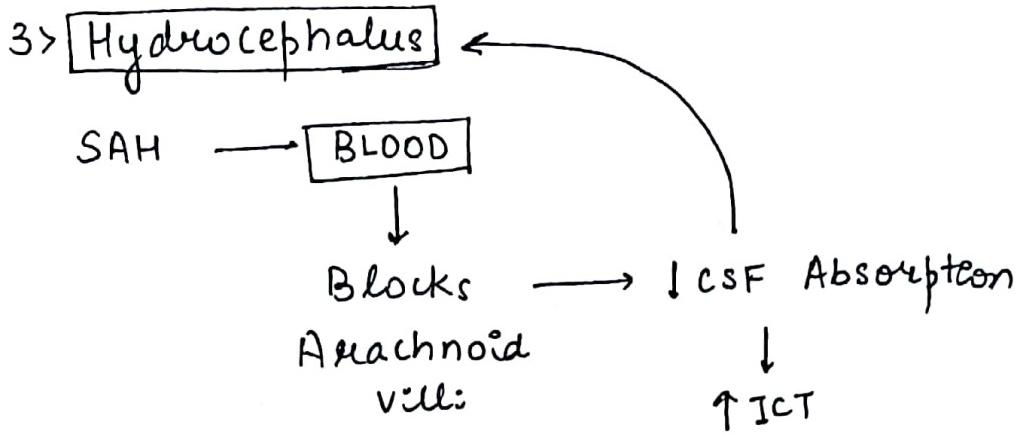
2) **Re-rupture**



may  
rebleed  
if  
undetected

30% re-rupture in 1st month

Peaks in 1st 7 days.



### INVESTIGATIONS

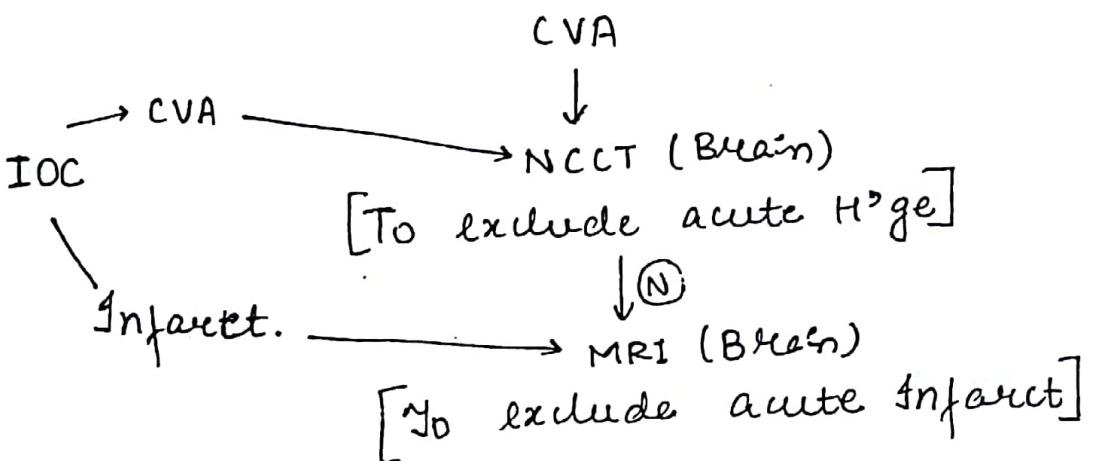
#### NEUROIMAGING

**CT**

Acute H<sup>o</sup>ge (clot)  
calcified

**MRI**

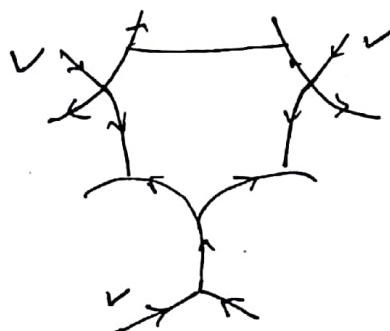
Inflammation  
Infarction  
Ischaemia



IOC

Acute SAH = NCCT (Brain)

Aneurysm = ANGIOGRAPHY



DYE  $\xrightarrow{\ominus}$  MR angio  
 $\xrightarrow{+}$

4 vessel angio  
 $\downarrow$   
 Injected

2 ICA  
 2 VA

$2 \text{ ICA} + 1 \cdot \text{VA}$ .  
 via femoral vein

Digital Subtraction Angiography (DSA)

subtract Bone

Rx

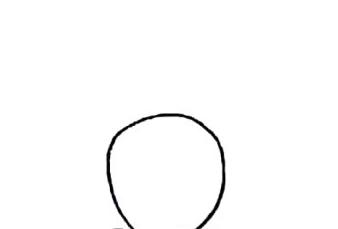
SURGICAL

TITANIUM

↑  
 clipping

PLATINUM

↑  
 coiling (BETTER)



WIDE NECK = clipping

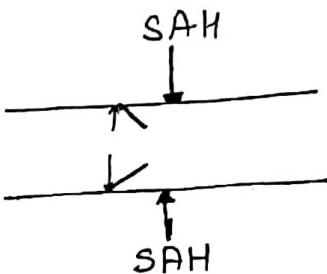


narrow neck = coiling

⇒ NIMODIPINE → Vasospasm

↓  
Intracerebral

⇒ 3H → HTN [160/90]  
Hyperolemia  
Hemodilution  
(I.V. fluid)



### SDH

occurs due to rupture  
of cortical Bridging  
Veins

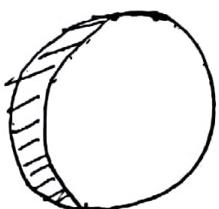
EDH  
Rupture of middle  
meningeal artery (MMA)

HEAD  
INJURY (closed)

↓  
Headache  
+ neurological  
Deficit

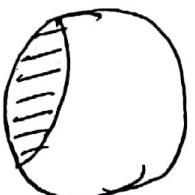
Progresses

Days - weeks - months  
slowly

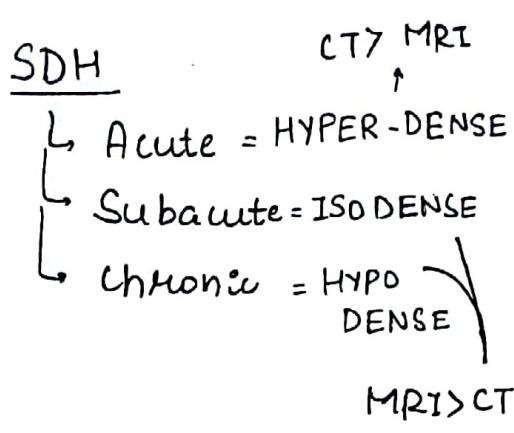


SEMITLUNAR

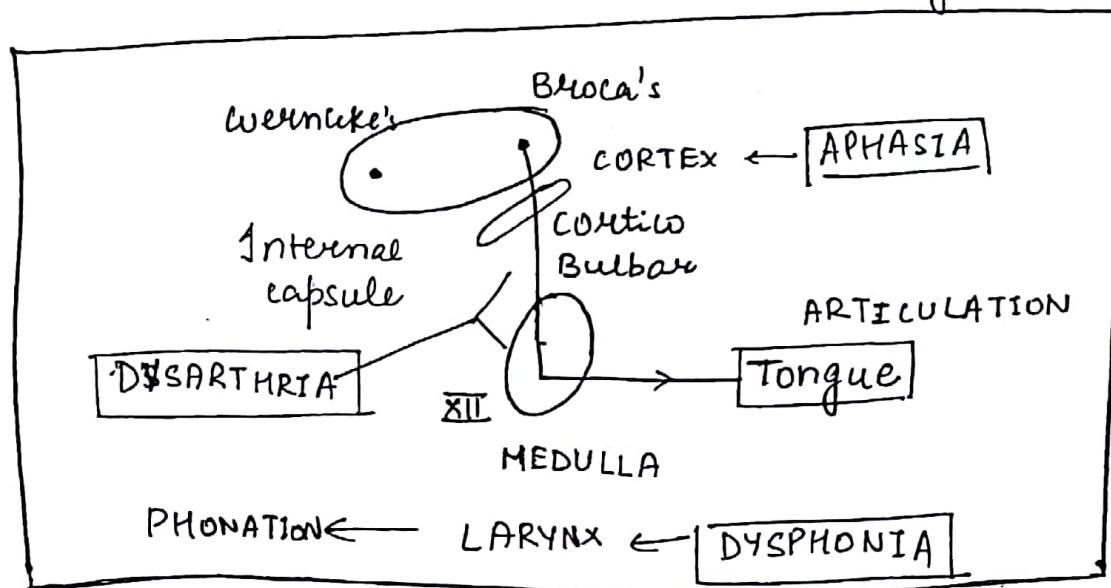
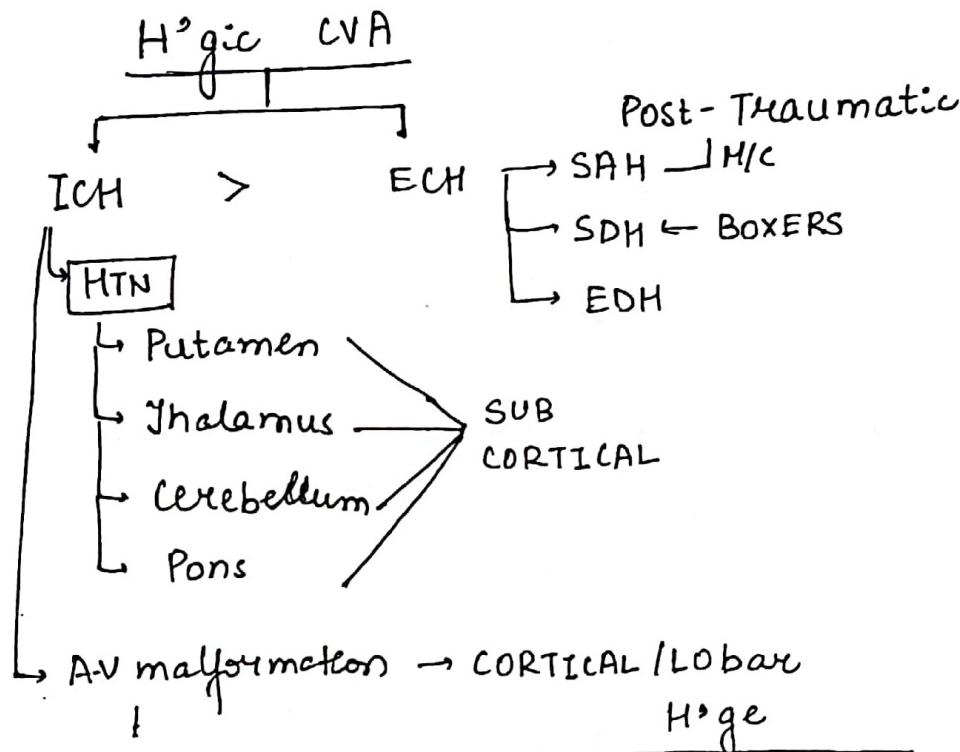
Hours - minutes  
Rapidly



LENTICULAR

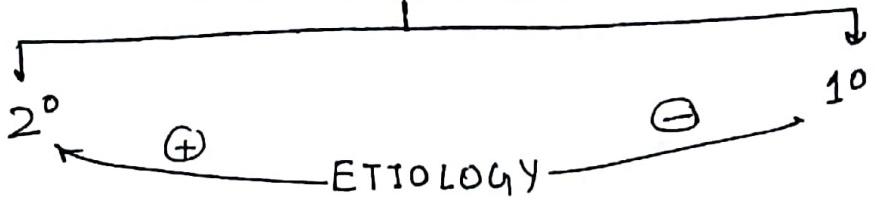


LUCID INTERVAL = **EDH**



# HEADACHE

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## TEMPORAL ARTERITIS

Elderly

♀ > ♂

Headache → Throbbing  
Stabbing

Scalp Tenderness → touching inflamed artery

Jaw claudication [SPECIFIC]

↳ Difficulty in chewing food

Blindness ← irreversible

↳ due to involvement of post cerebral  
artery

Inv-

↑ ESR

, Biopsy → Temporal Artery Biopsy

↓

Giant cells

Rx - DOC = STEROIDS

PSEUDO TUMOUR CEREBRI / BENIGN IDIOPATHIC INTRACRANIAL HTN

H/c - young obese, ♀

Headache

Projectile vomiting (nausea Ⓛ)

Papilloedema

Ventricle size N

No focal neurological Deficit

↓ CSF Absorption.

ETIOLOGY

- 1) Hypervitaminosis A
- 2) Expired Tetracycline
- 3) OCP
- 4) Steroid withdrawal (Abrupt)

H/C/C  
↓  
Idiopathic

Rx = ACETAZOLAMIDE

↓ CSF formation.

TENSION HEADACHE

♀ > ♂

H/c 1° Headache = Tension Headache

Associated with DEPRESSION

Tension is not an etiology

Dull Aching Pain

Band like



EPISODIC → < 15 day/mnth = ANALGESICS

Rx ↙ CHRONIC → > 15 day/mnth = T.C.A. ↘ Rx ↗  
Amytryptiline

# MIGRAINE

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♀ > ♂

4-72 hours

$\geq 2$

|                                     |
|-------------------------------------|
| P → Pulsatile                       |
| U → U/L                             |
| M → Moderate to severe in intensity |
| A → aggravation                     |

+ any 1      ↗ nausea (H.c.)  
                 ↗ Vomiting

or    any 1      ↗ Photophobia  
                 ↗ Photophobia

AURA = visual > sensory



CLASSICAL (20%)

COMMON (80%)

ACCEPTED      THEORY

① Cortical Spreading Dissociation

Main Trigger → vasoconstrictive → [SCOTOMA]

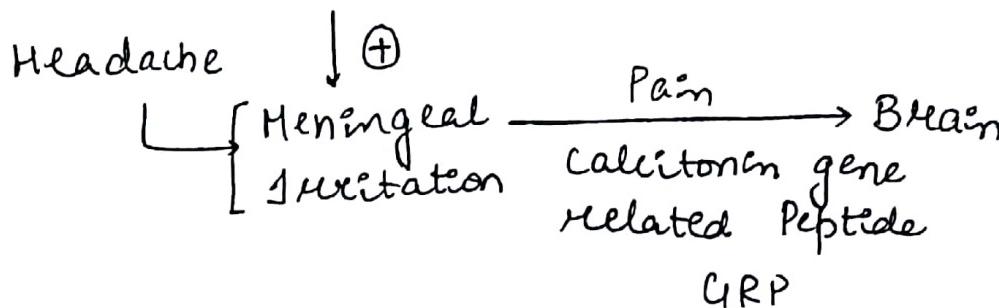
↑  
Intracranial (occipital)

↓  
vasodilatation → FLASHES OF LIGHT

FORTIFICATION  
SPECTRA

vasodilation

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② SEROTONINERGIC

[5HT  $\ominus$ ]  $\Rightarrow$  throbbing

Rx = 5HT  $\ominus$

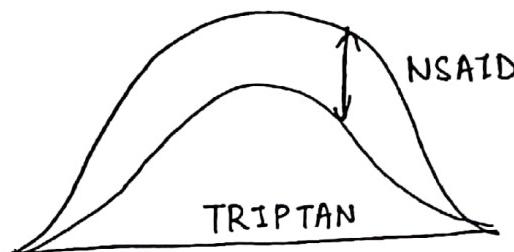
NON SELECTIVE  $\rightarrow$  ergotamine

SELECTIVE  $\rightarrow$  1B/1D

[Triptans]

DOC for acute attack

RIZA triptan > SUMA triptan



③ DOPAMINERGIC  $\longrightarrow$  DA  $\ominus$

DA  $\oplus$   $\rightarrow$  nausea

Metoclopramide

PROPHYLAXIS  $\times$  5-6 months

① B  $\ominus$   $\Rightarrow$  Propranolol (widely used)

② TCA  $\Rightarrow$  Amitriptyline

③ CCB → Flunarizine

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④ A.E.D. → Valproate  
Topiramate  
Gabapentine

Ethosuximide

Not Recommended.

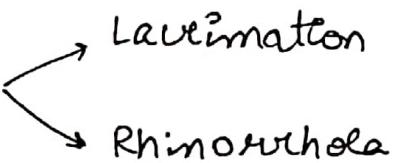
## CLUSTER HEADACHE

♂ > ♀

Peri / Retro orbital Pain

- U/L
- 30 min - 2 hours
- ppt. by consumption of alcohol
- awakens from sleep.

Autonomic ↑  
hyperactivity



Rx = O<sub>2</sub> inhalation (Rxoc)

② 10-12 L/min × 10-15 min

Prophylaxis = Verapamil (Dol)

(lifelong)

# PAIN

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## SENSITIVE

- Circle of Willis
- Meningeal arteries
- Dural sinuses/veins

## INSENSITIVE

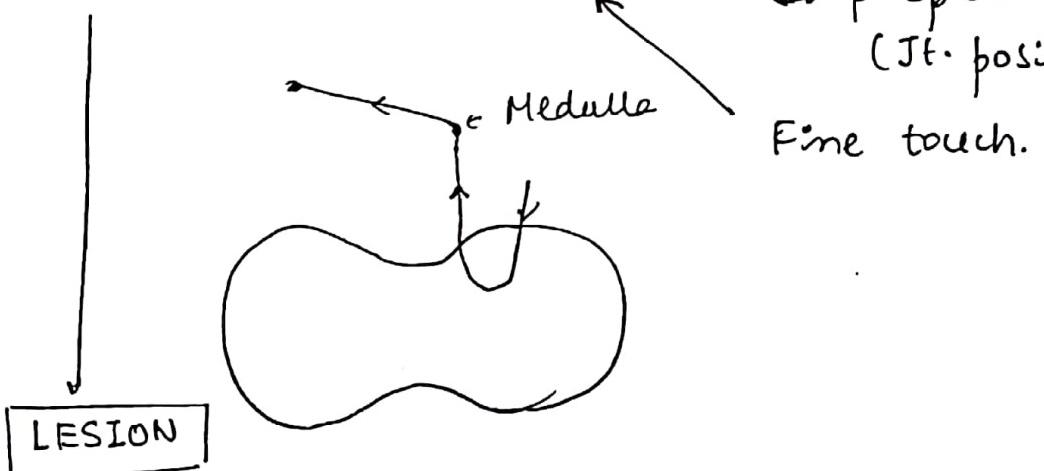
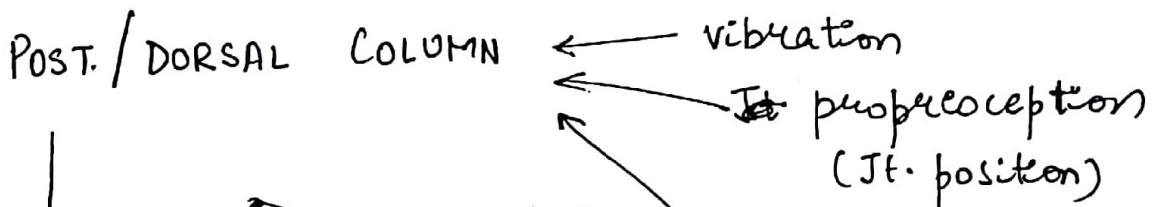
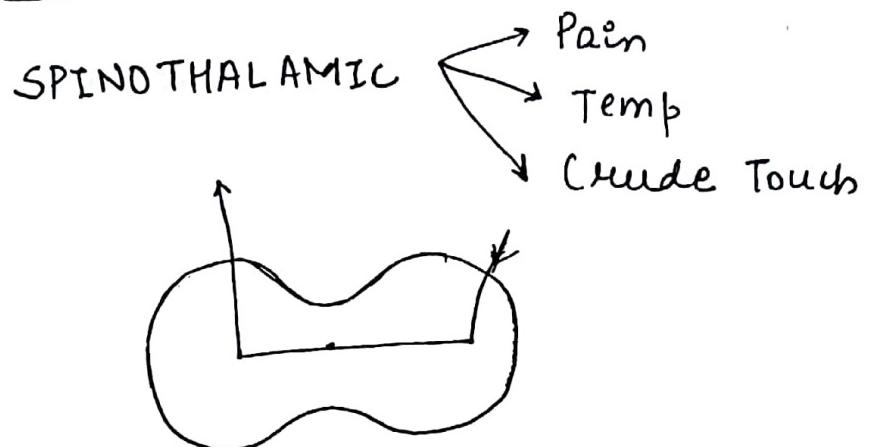
- Duramater
- Arachnoid Mater
- Choroid Plexus
- Ventriculare Ependyma

## D/D of MIGRAINE

- 1) Glaucoma



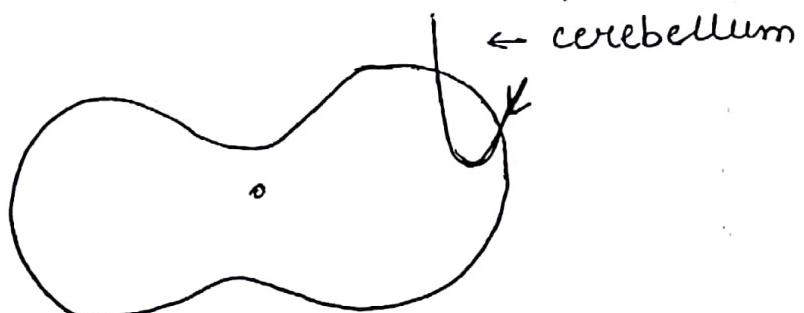
## ASCENDING / SENSORY



↳ Stamping Gait  
 ROMBERG's TEST      (+) → sways  $\approx$  eyes closed

## SPINOCEBELLAR TRACT

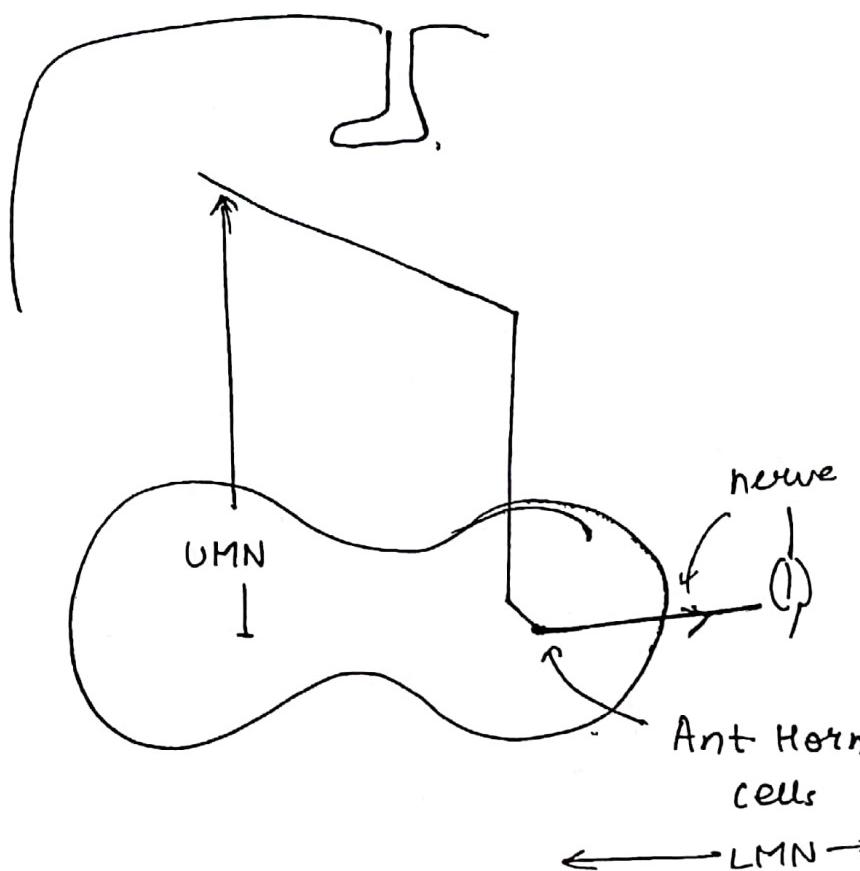
↳ subconscious proprioception



## DESCENDING TRACT

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## CORTICOSPINAL TRACT



## PARALYSIS

### UMN

Tone ↑ (spasticity)

DTR brisk

Plantar extensor  
[Babinski +]

### LMN

↓ (flaccidity)

Dull / absent

wasting / atrophy ↗

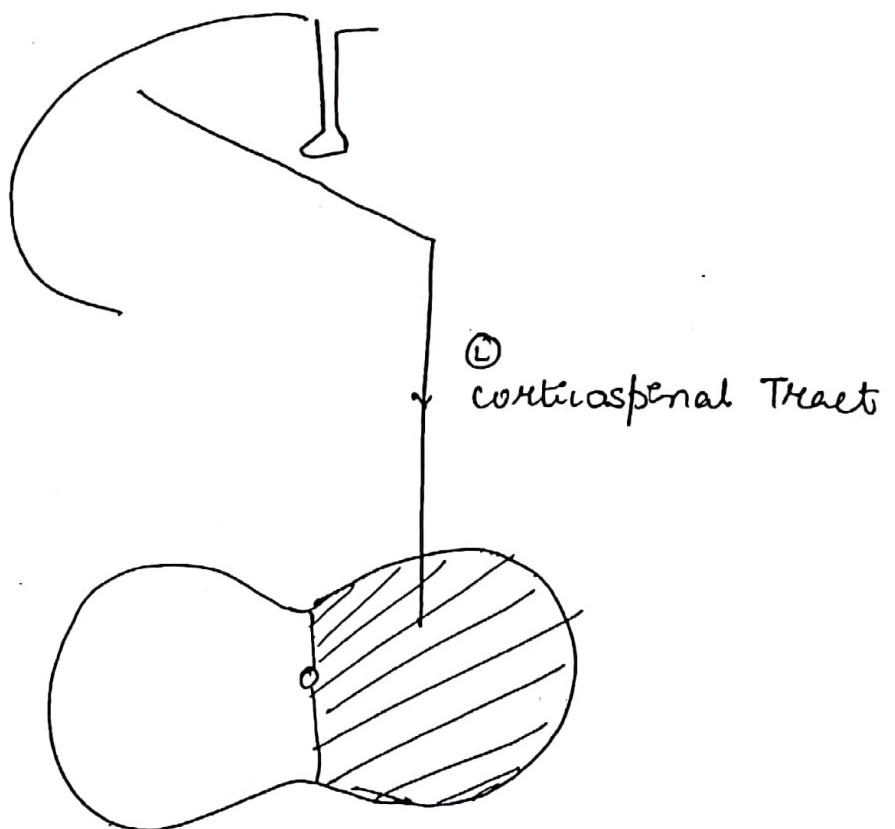
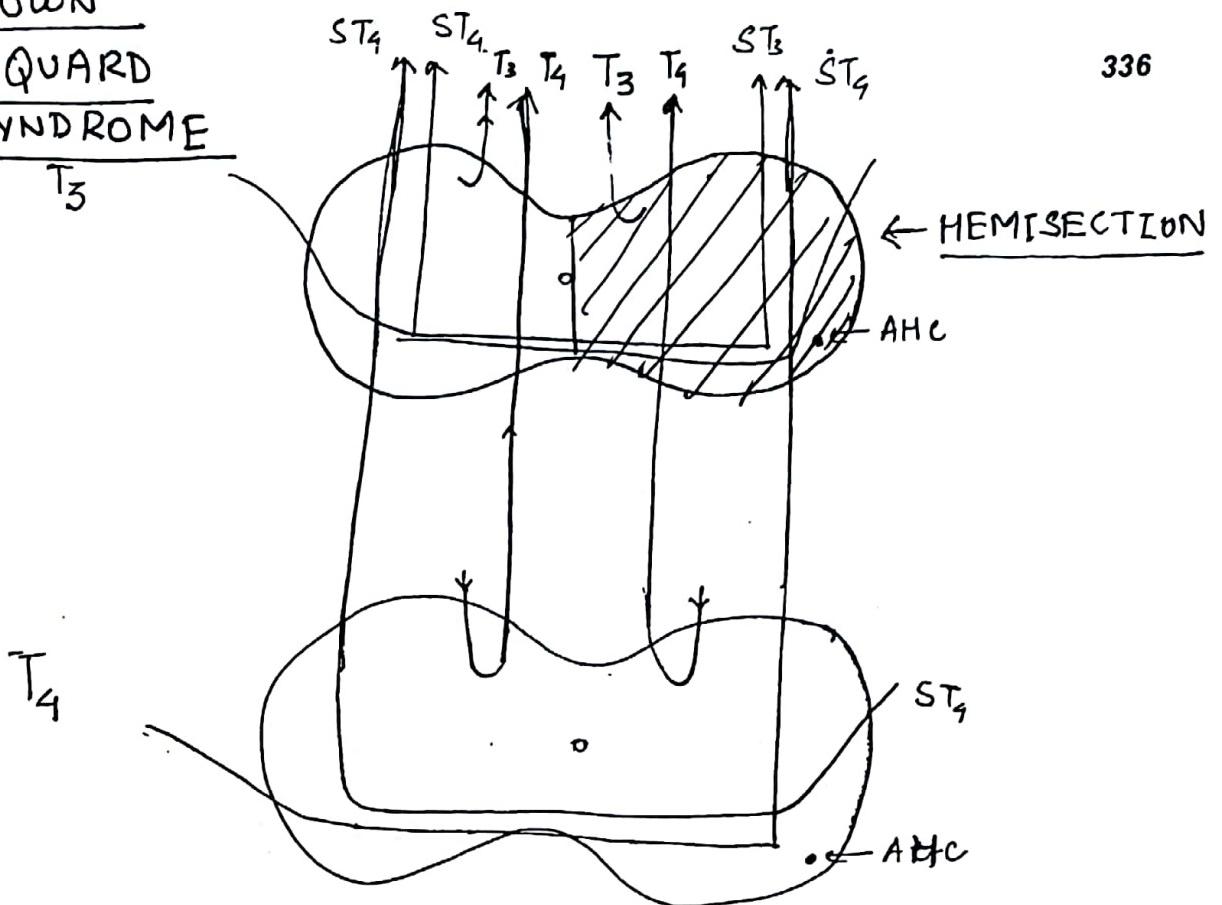
Fasciculation

Twitch → visible  
PALPABLE  
LESSON

↳ Ant. Horn cell.

BROWN  
SEQUARD  
SYNDROME

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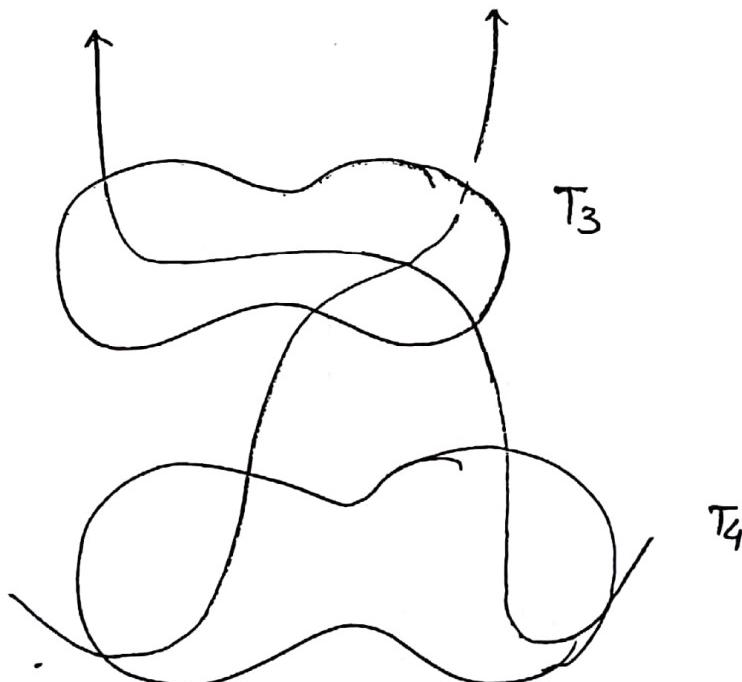
## HEMISECTION of T<sub>3</sub>

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At T<sub>4</sub> → ~~FL~~ Loss of Spinothalamic → C/L  
Post-column → I/L  
weakness → UMN  
I/L.

At T<sub>43</sub> = P Loss of Post column - I/L  
weakness - LMN, I/L

\*\* Spinthalamic - I/L



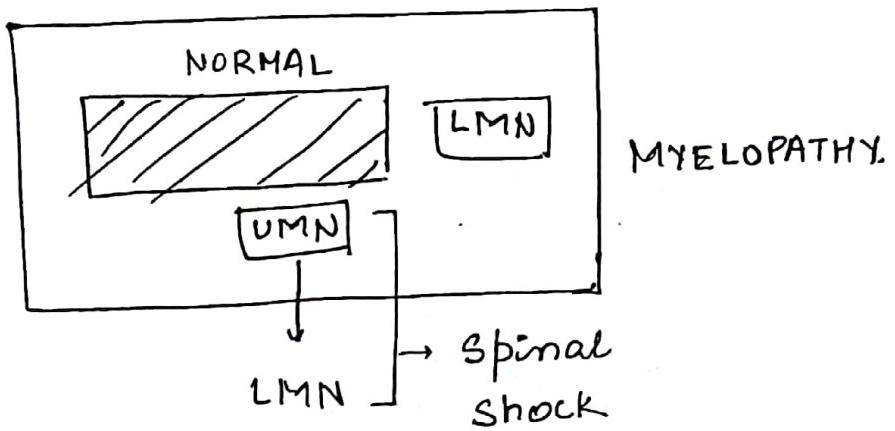
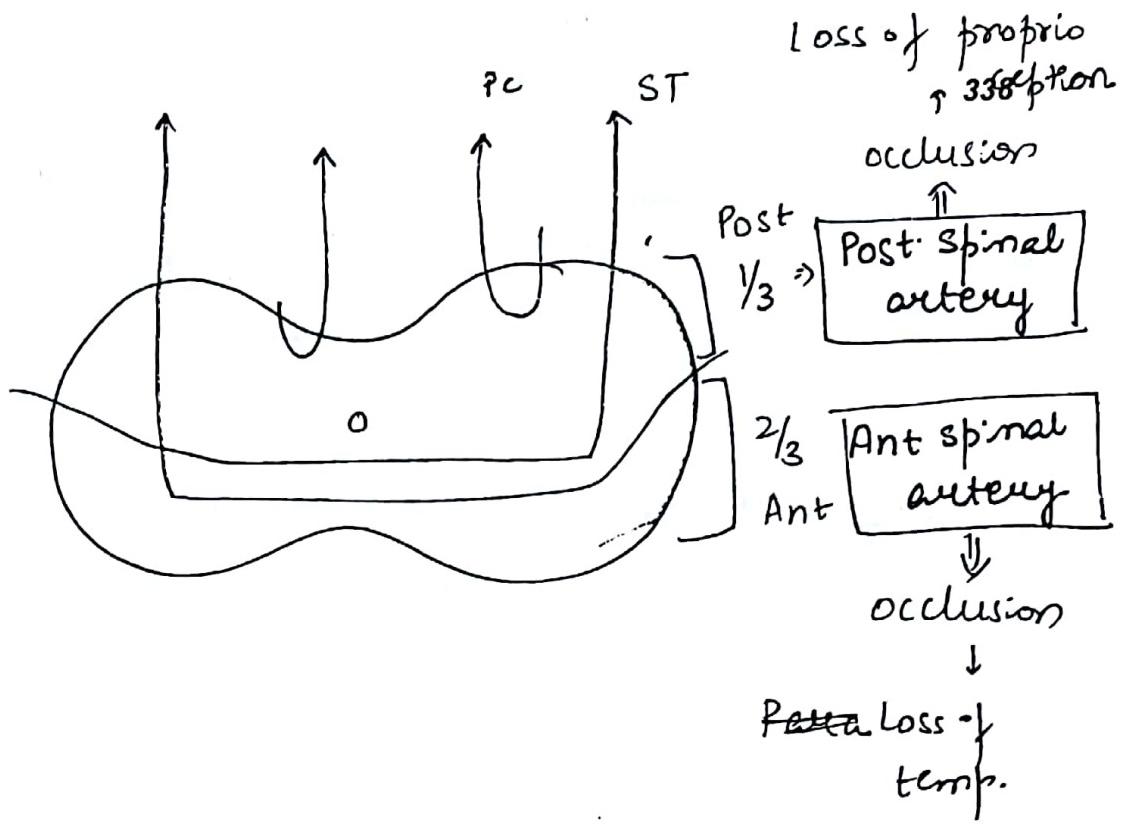
AT THE LEVEL ⇒

Spinothalamic  
Post. column → SAME  
LMN SIDE

~~ABOVE~~ BELOW The LEVEL ⇒

Spinothalamic  
↓ opposite side.

P. C. → same side  
UMN



## QQ SPINAL SHOCK

**Transient** LMN weakness below the level of lesion



most occurs

② 48-72 hrs

- Flaccidity
- Areflexia
- Urinary retention.

→ sensory Loss

→ **wasting** (⊖)

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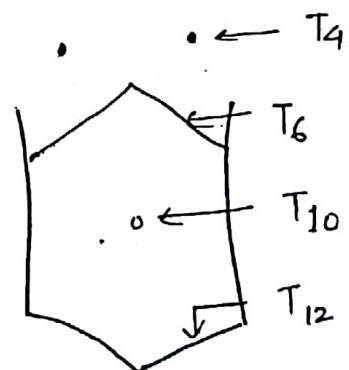
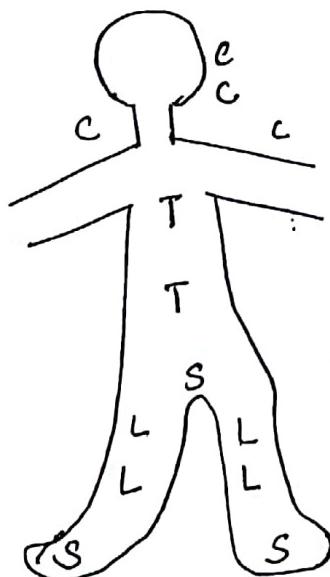
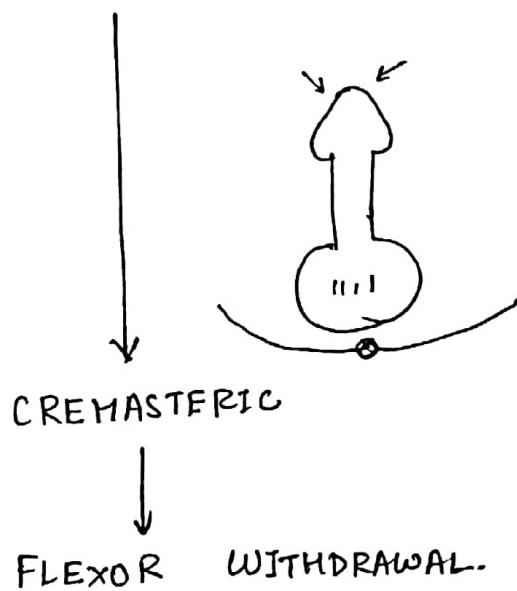
Transient process

internal nutrition is intact

Spinal shock = LMN - wasting

1st Reflex Recovery-

BULBOCAVERNOUS. → EXTERNAL ANAL SPHINCTER.



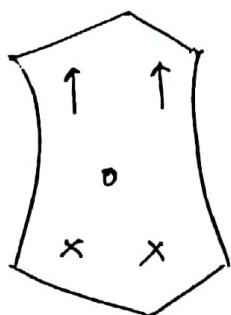
BEEVOR SIGN



**BEVOR SIGN**

Supine → Sitting position

If umbilicus moves upward ⇒ Lesion @/below T<sub>10</sub>

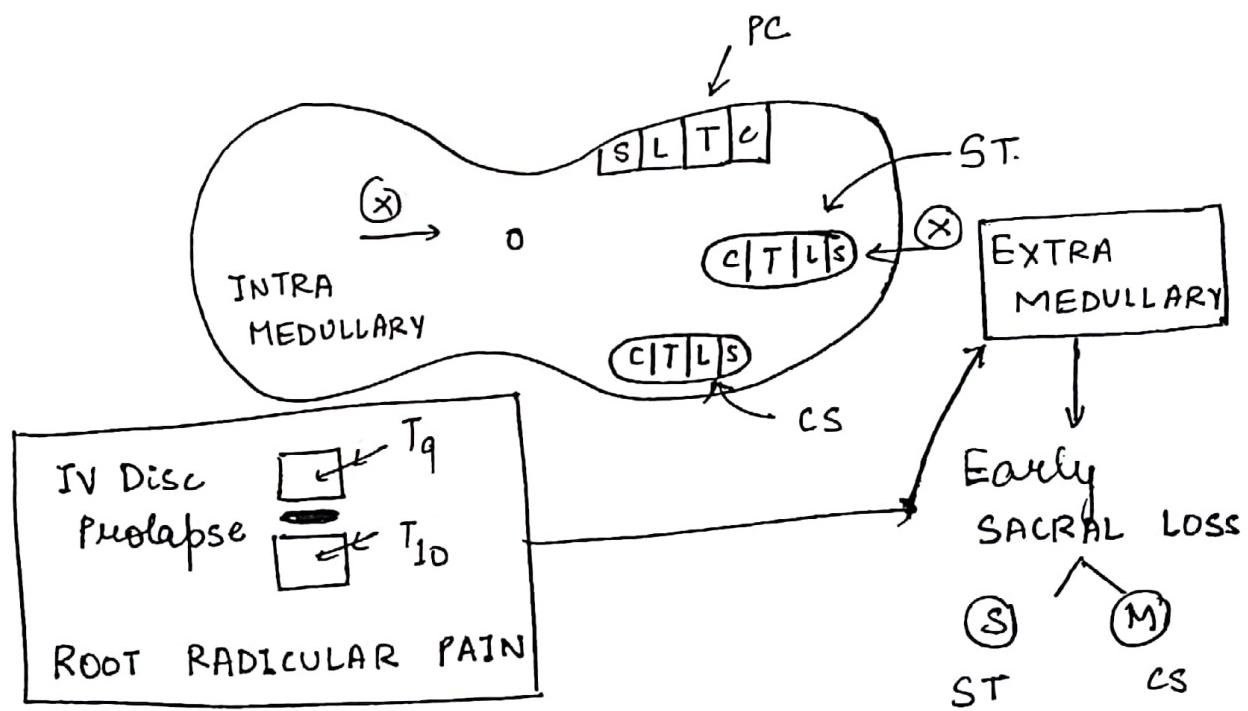


**PRONATOR DRIFT SIGN**

weak side

PRONATION + ↓ DRIFT

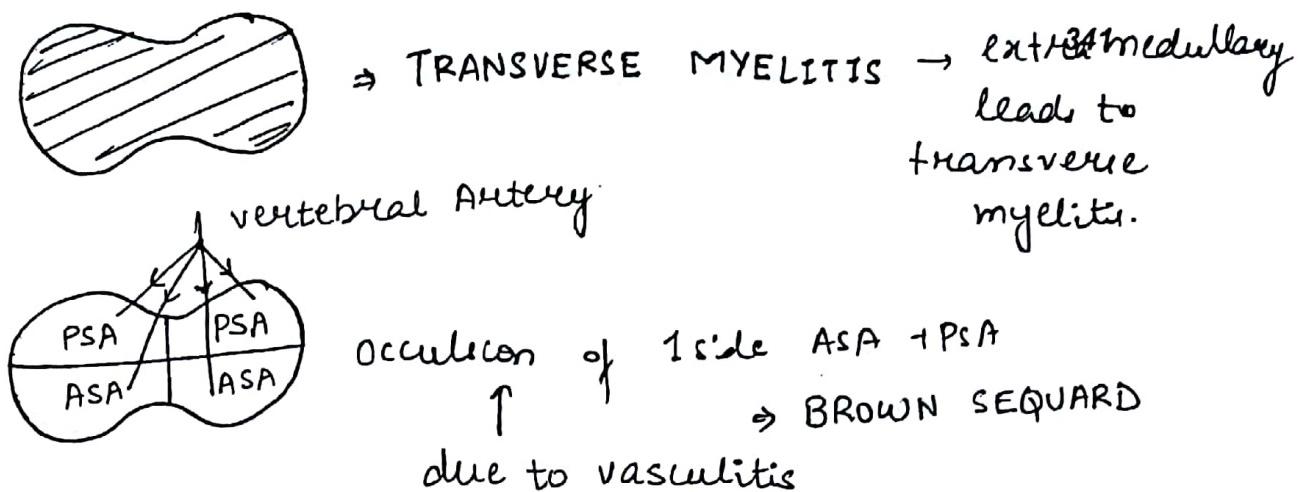
Injury CS tract  
CVA in evolution.



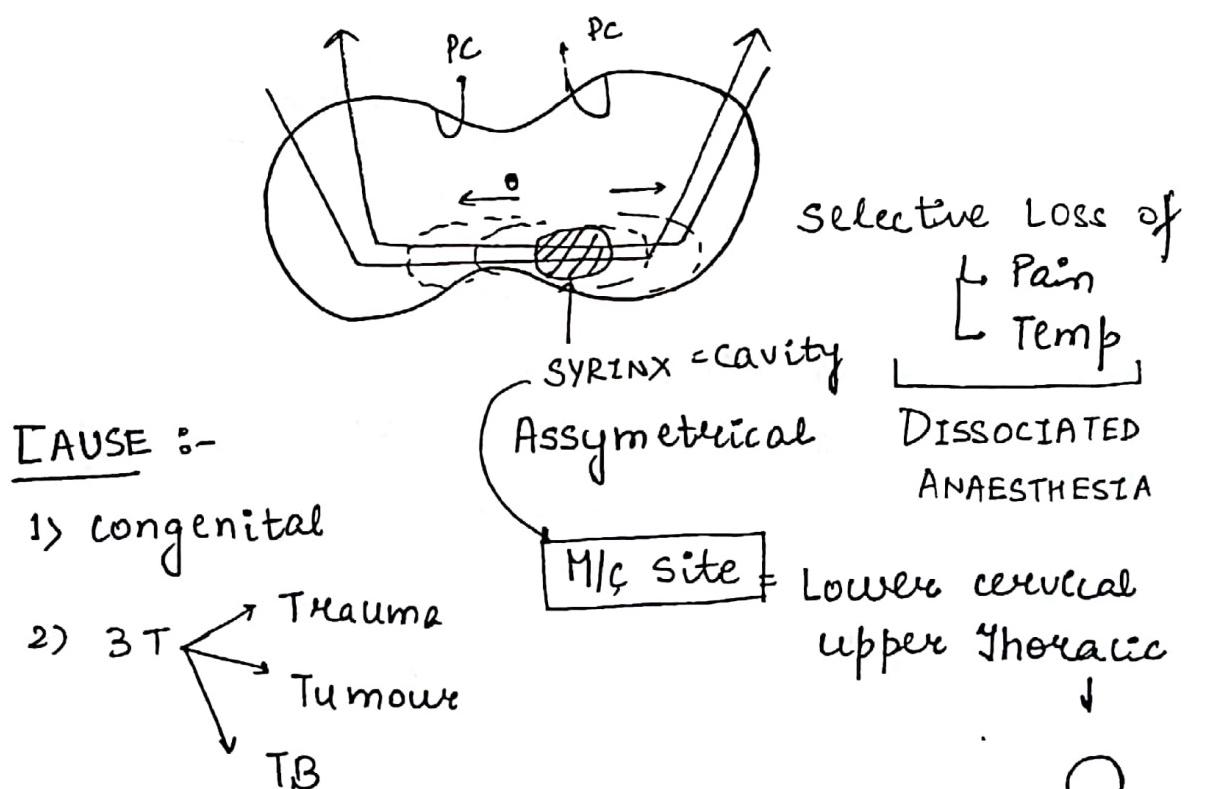
Descending → (S) }  
→ (M) } LOSS

Burning Pain ⊕

Ascending → (S) }  
→ (M) } LOSS

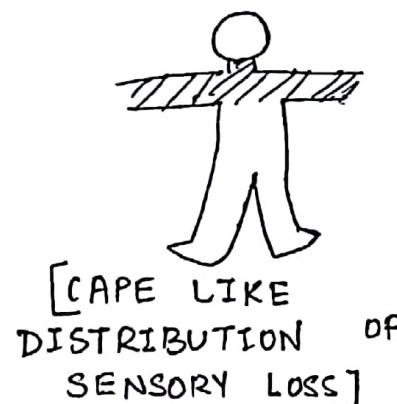


## QQ SYRINGOMYELIA



AT THE LEVEL → LMN weakness

Below the level → UMN weakness



CHIARI MALFORMATION > 50%  
(Type 1)



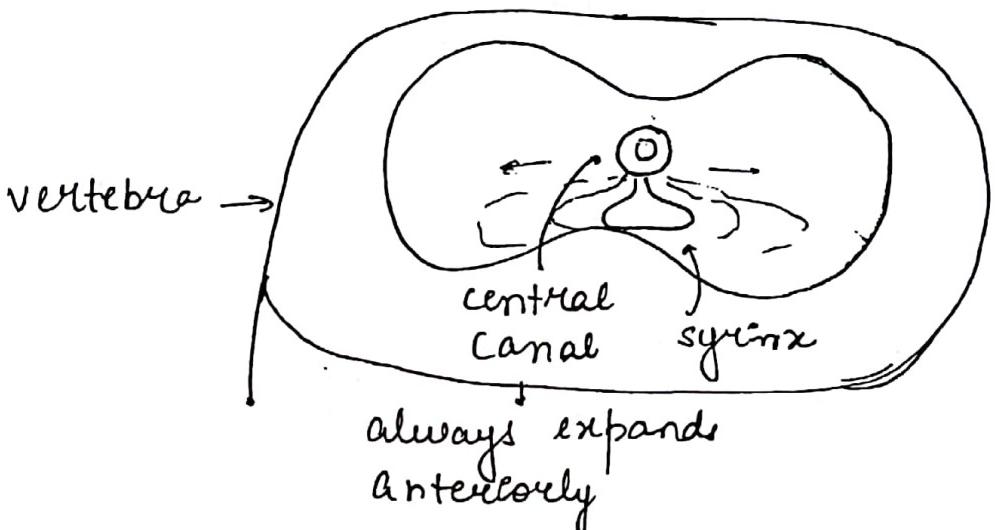
Cerebellar tonsillar herniation into foramen  
Magnum



compresses central canal containing CSF



it starts enlarging due to compression



Rx = DECOMPRESSION LAMINECTOMY

| to relieve pressure on ~~the~~ expanding  
| spinal cord from vertebra

#### DISAD

↳ doesn't relieve symptoms.

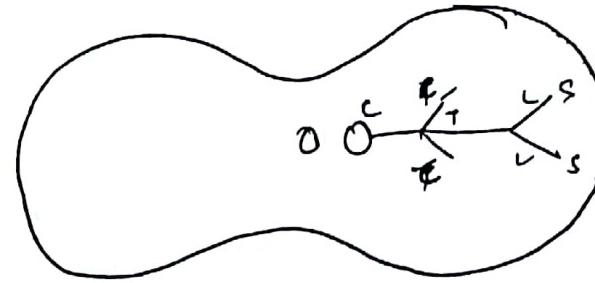
NOTES (c/f of syringomyelia)

→ Painless burning of hands occur early

↓  
Trophic ulcers

→ absent biceps jerk ( $C_5, C_6$ )

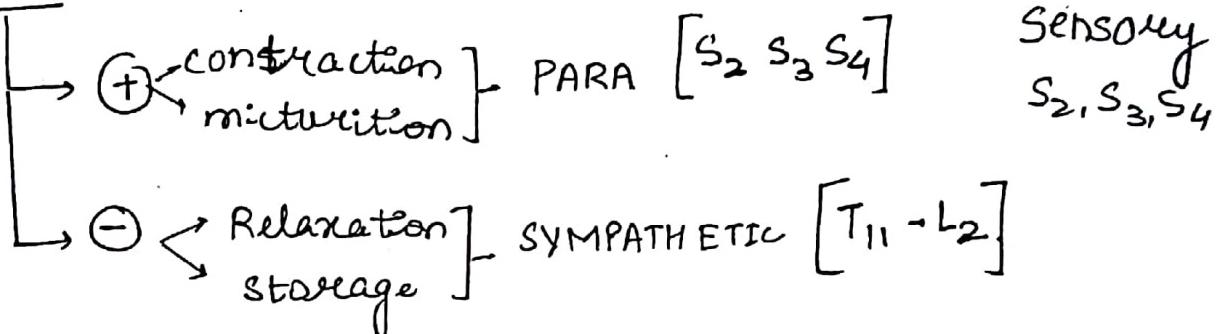
→ extensor plantaris [ $L_5, S_1$ ]



## URINARY BLADDER

FRONTAL (Paracentral lobule) where  $\Rightarrow$  ACA

PONS CENTRE



[A]  $S_2 S_3 S_4$  (-) [AUTONOMOUS BLADDER]

$S_2 S_3 S_4$   
 $\rightarrow$  (-)  $\rightarrow$  sensory  
 $\rightarrow$  Para

$T_{11} - L_2$

++ L Sympathetic

HYPOTONIC  
FLACCID  
LARGE CAPACITY  
OVERFLOW  
INCONTINENCE

[B]  $T_{11} - L_2$  ⊖ [AUTOMATIC BLADDER]

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$T_{11} - L_2$

⊖ Symb

$S_2, S_3, S_4$

++ < sensory  
parasymp

- HYPER TONIC
- SPASTIC
- LOW CAPACITY
- URGE INCONTINENCE

CONUS MEDULLARIS



S.C. ends opp. to  
 $L_1, L_2$ .

$S_1 - S_5$  segments

KNEE JERK

$L_3 - L_4$  ++ [N]

ANKLE - JERK

$S_1 - S_2$  ⊖

BLADDER

AUTONOMOUS  
(early)  
Intra

CAUDA EQUINA



nerve Roots

$L_1 - L_5$   
 $S_1 - S_5$

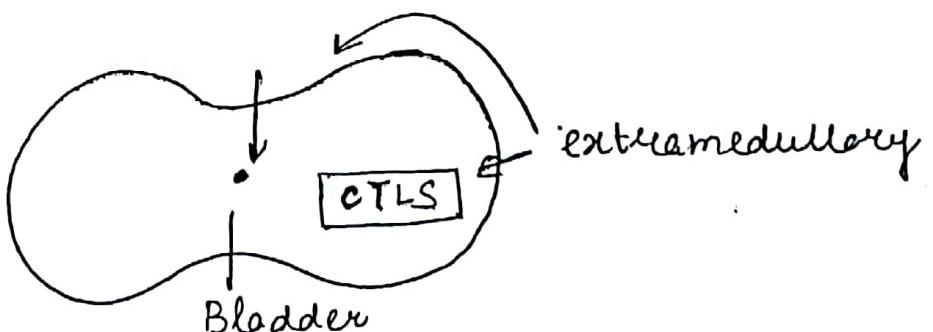
⊖

⊖

MIXED (NEUROGENIC)

(Late)

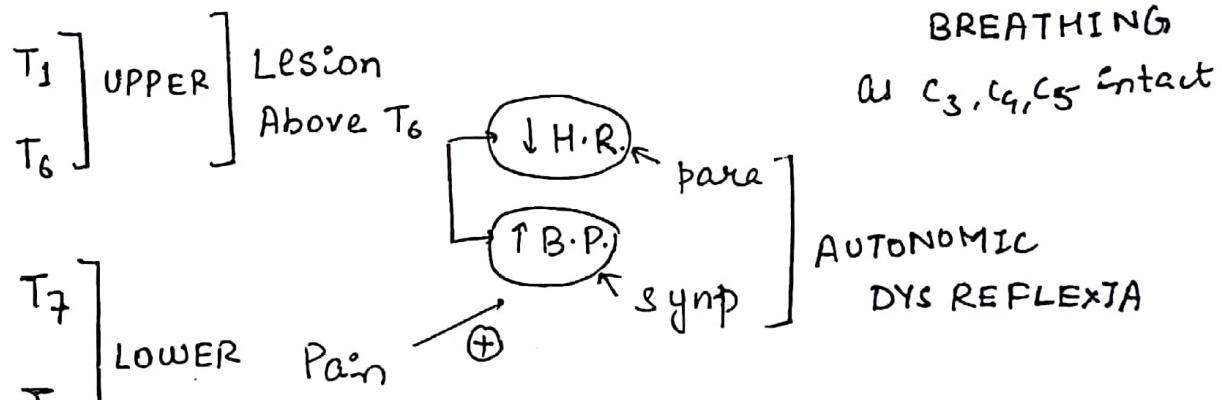
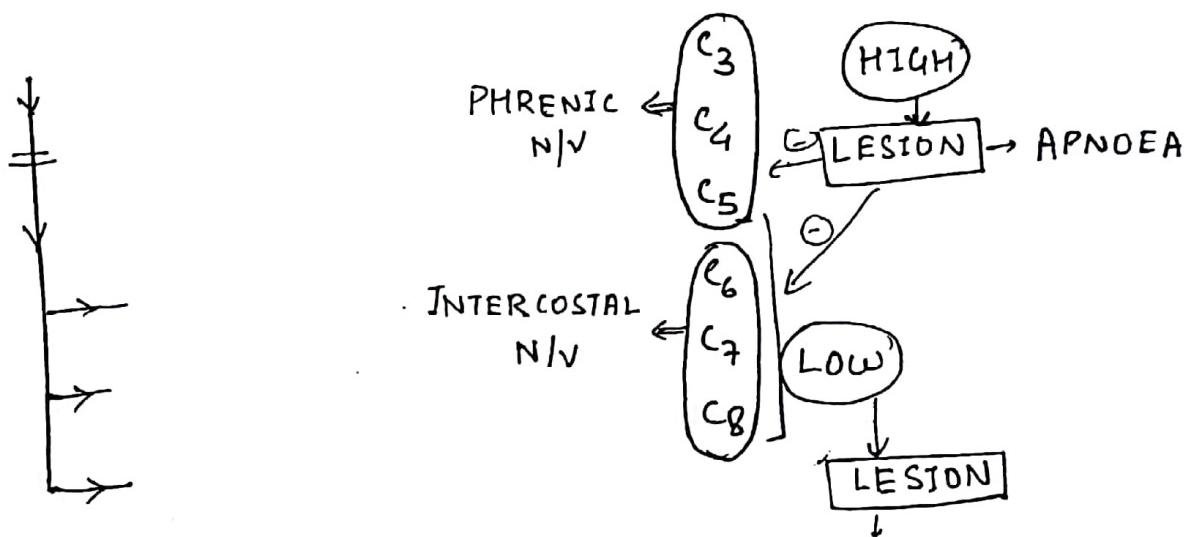
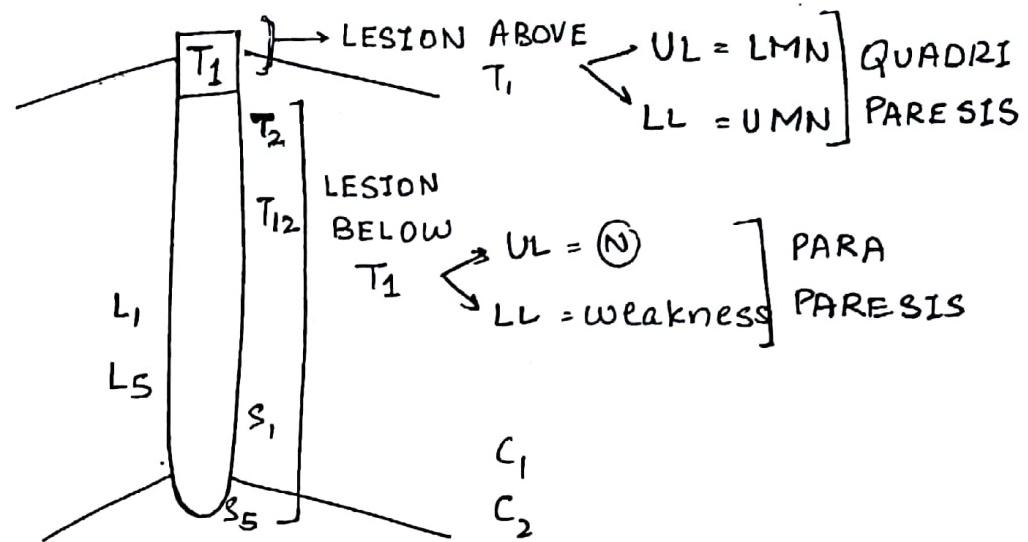
↑  
extra



Asymmetrical

Areflexic

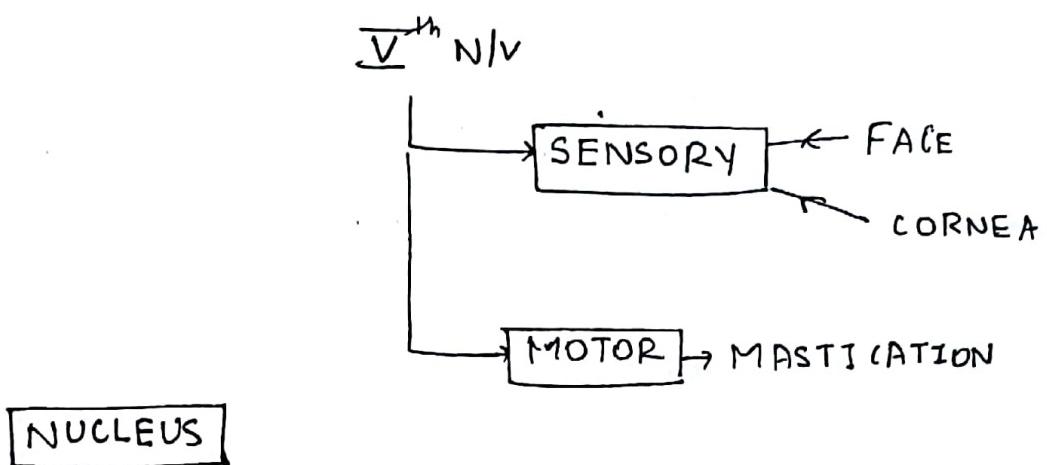
LMN Paralysis



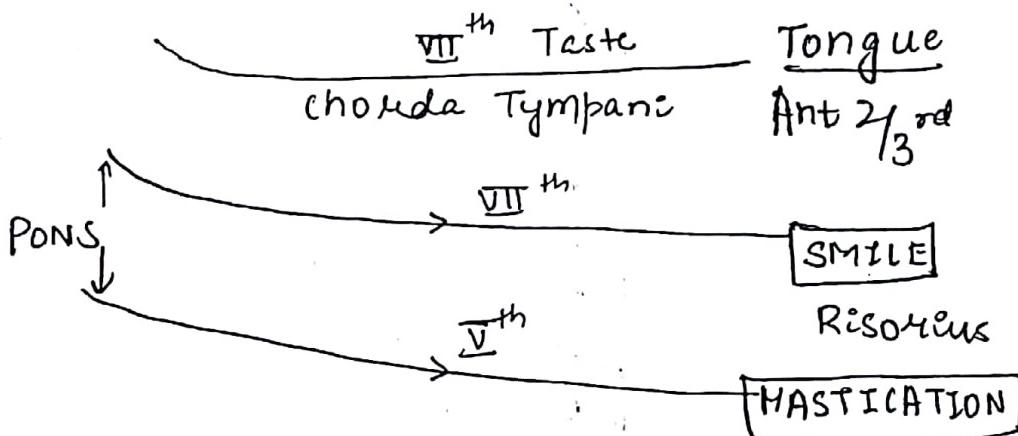
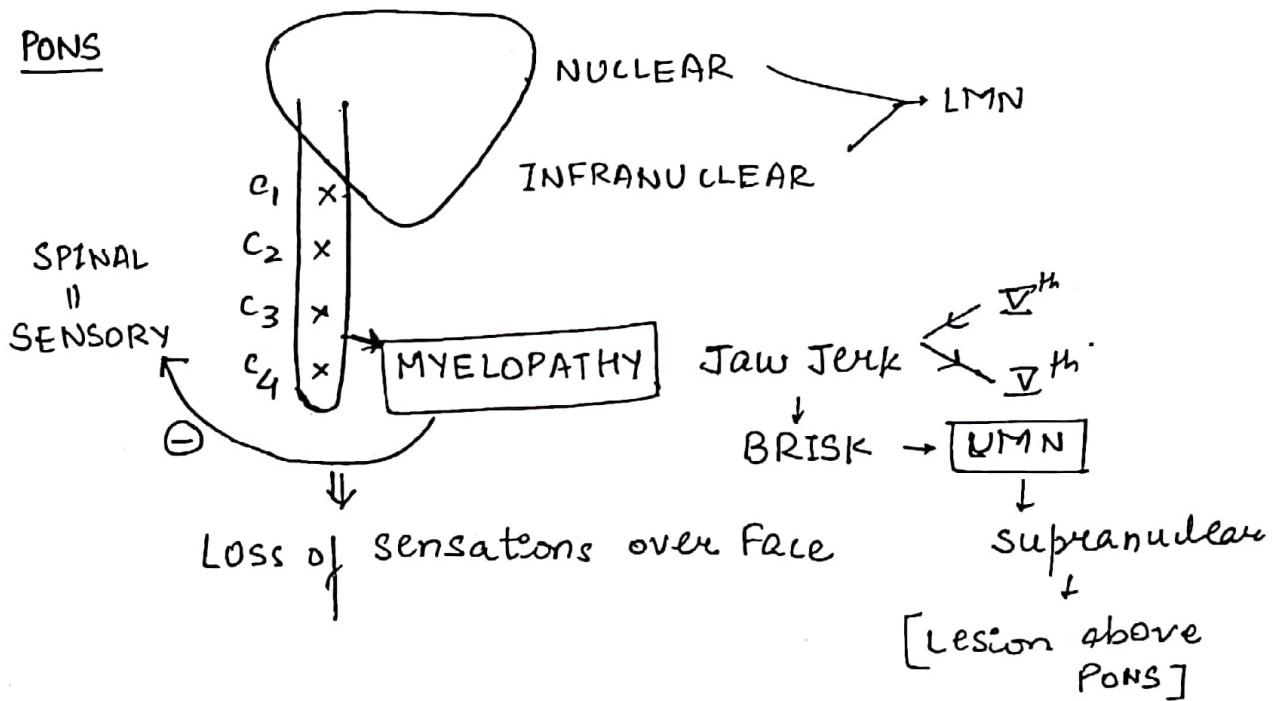
R<sub>x</sub> = **NIFEDINE**  
**CLONIDINE**

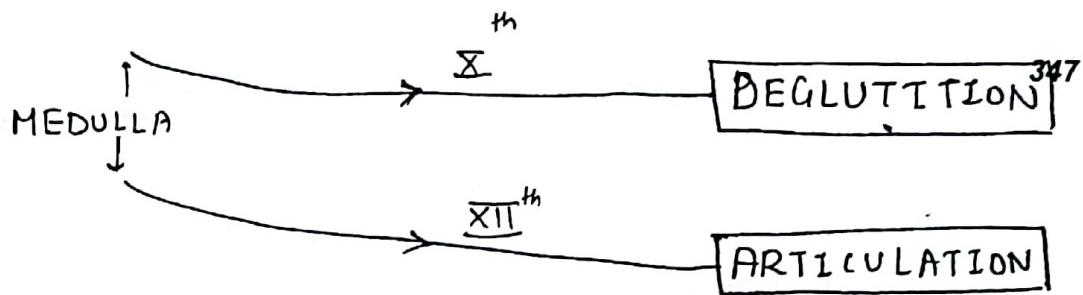
# TRIGEMINAL N/V

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SUPRANUCLEAR → UMN





### FACIAL N/V

TRIGEMINAL      NEURALGIA

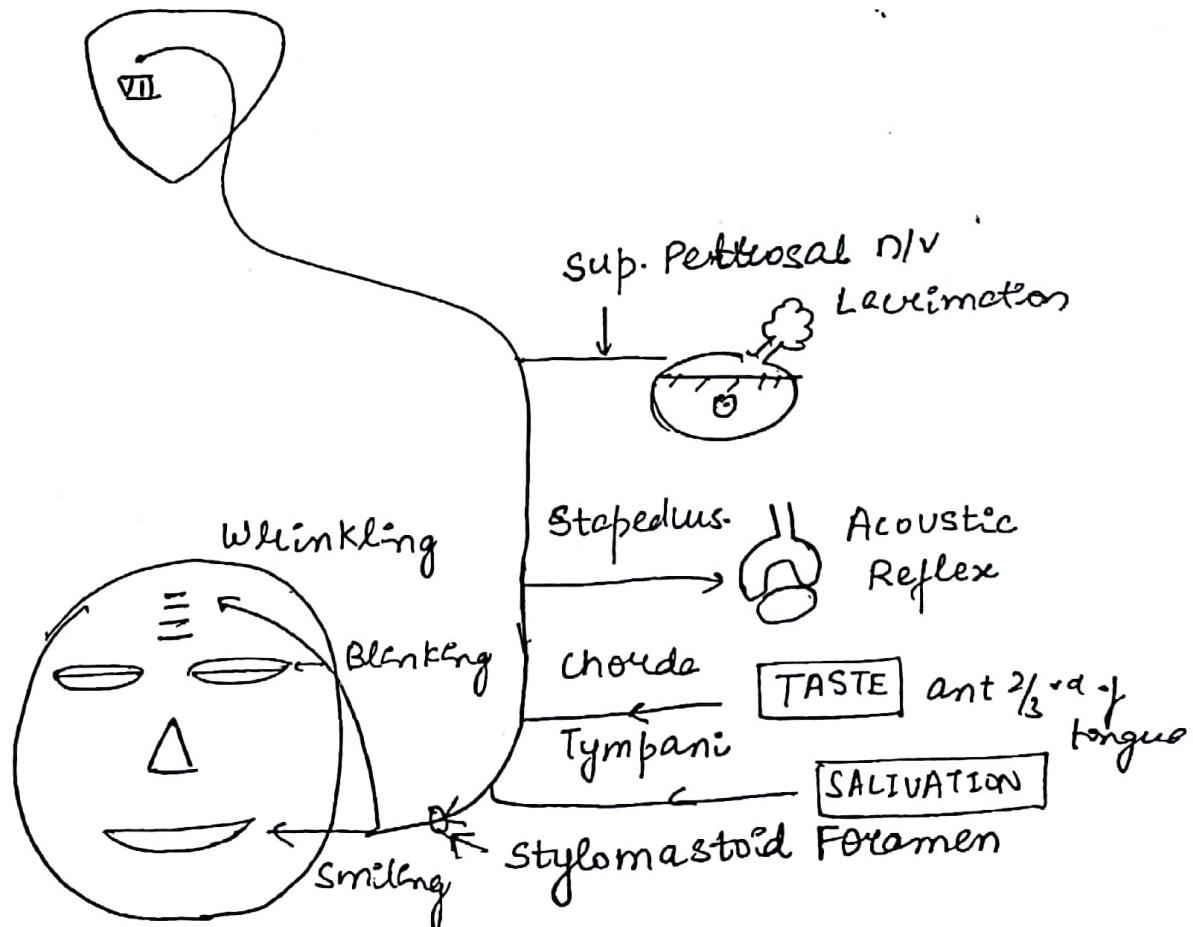
Electric shock on Face / TIC DOLOREUX

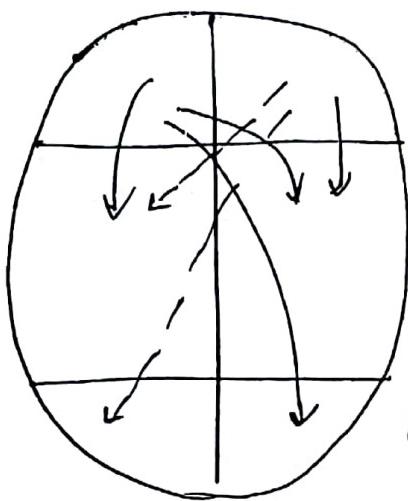
Rx → Inject<sup>n</sup> of C<sub>2</sub>H<sub>5</sub>OH / glycerol in Gasserian ganglion

RHIZOTOMY - Radio Frequency Ablation

### FACIAL N/V (VII<sup>th</sup>)

#### PONS

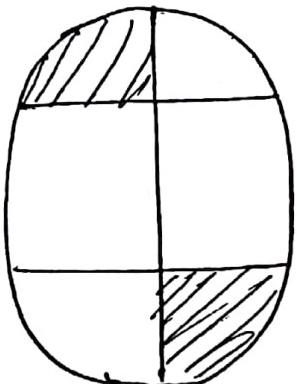




Upper  $\frac{2}{3}$ rd Face is having B/L corticocortical innervation

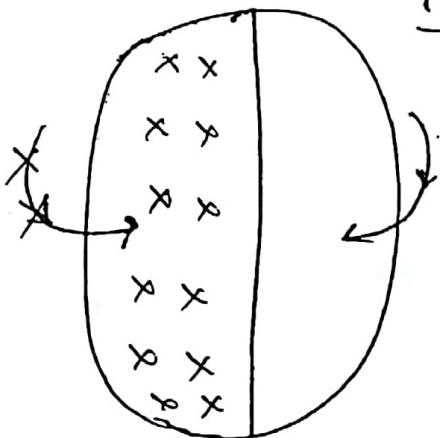
Lower  $\frac{1}{3}$ rd of Face supplied by opposite cortex

A&gt;



CORTICAL LESION  $\Rightarrow$  UMN PARALYSIS  
(subcortical)

B&gt;



PONS LESION  $\Rightarrow$  LMN PARALYSIS

U/L  $\rightarrow$  CAUSE

1) Trauma

2) Herpes zoster virus

[RAMSAY HUNT SYNDROME]

3) Idiopathia [BELL'S PALSY]

B/L

CAUSE

1) UBS

2) HIV

3) Sarcoidosis

## RECOVERY

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Aberant Reinnervation

1) CROCODILE TEAR SYNDROME

2) SYNKINESIA (smiling Blinking together)

H/o ⇒ S/O CERVICAL CORD INJURY

- 1) Fall from height
- 2) Road traffic accident
- 3) Hanging

## LHERMITTE SYMPTOM

MULTIPLE ON flexion of neck

SCLEROSIS

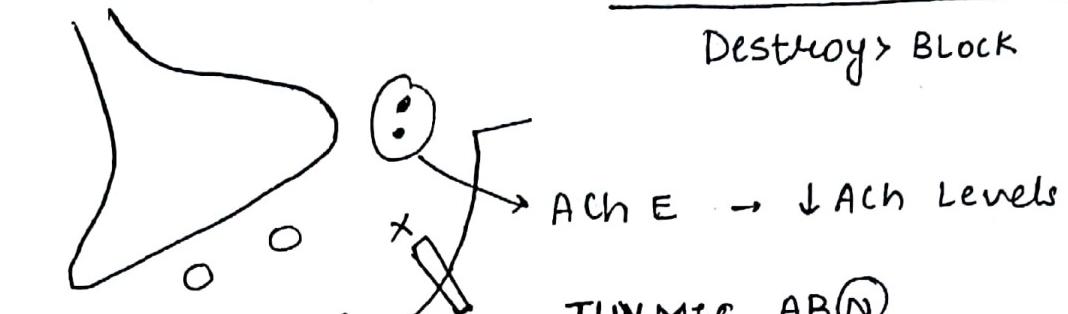
Pain / electric shock  
across spine

# MYASTHENIA GRAVIS

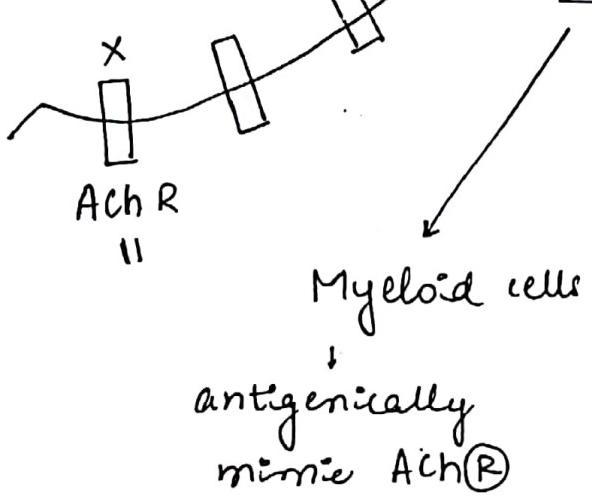
350

## ACh R<sup>(R)</sup> ANTIBODIES

Destroy > Block



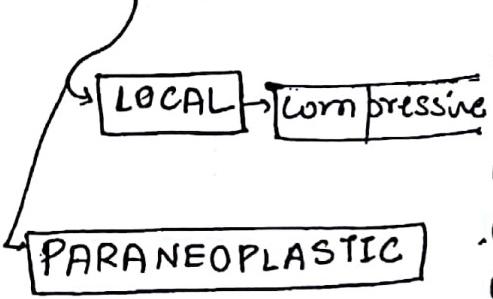
## THYMIC AB(N)



So, Antibodies cross react

↳ 75% Myasthenia Gravis

↳ 65% Hyperplasia  
↳ 10% Thymoma

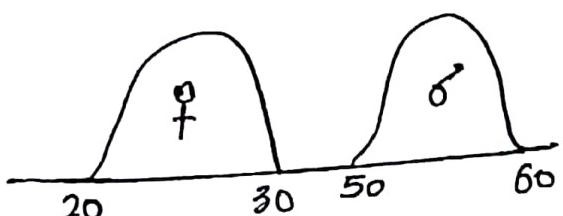


## PARANEOPLASTIC

MRI  
(chest)

Pure red cell Aplasia  
Pernicious Anemia  
Hypoγ globinemia  
Dermatomyositis

$$\text{♀} : \text{♂} = 3:2$$



3-7% MG

suffer from Hypothyroidism

So,  $\text{Inr} = \text{TSH}, 351$

C/F :-

1) easy fatigability

↳ Proximal

↳ Asymmetrical

2) OCULAR [1st m/s to involve]  
[M/C m/s to involve]

Ptosis

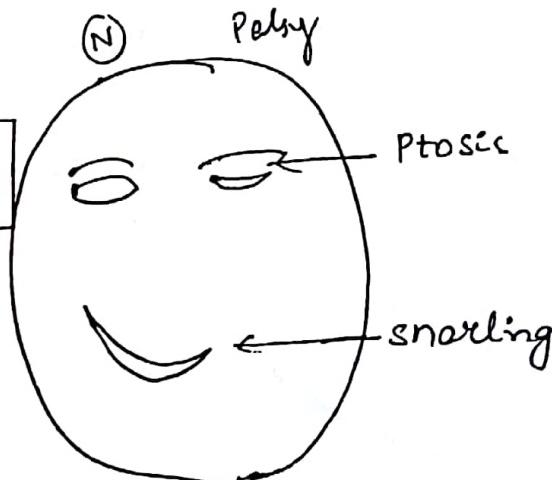
opthalmoplegia

2) FACIAL

snarling

↓  
can't maintain  
smile for long

PEEK  
SIGN



close eyes for some time then  
opens as if seeing through small  
aperture

3) SKELETAL

(N) → DTR

↳ sensory intact  
↳ Bladder  
↳ cognition

## 1) EDROPHONIUM / TENSILON TEST

↓  
shorter acting  
Peripheral action  
[BEST SCREENING TEST]

## 2) ACh R Antibodies

MOST SPECIFIC TEST

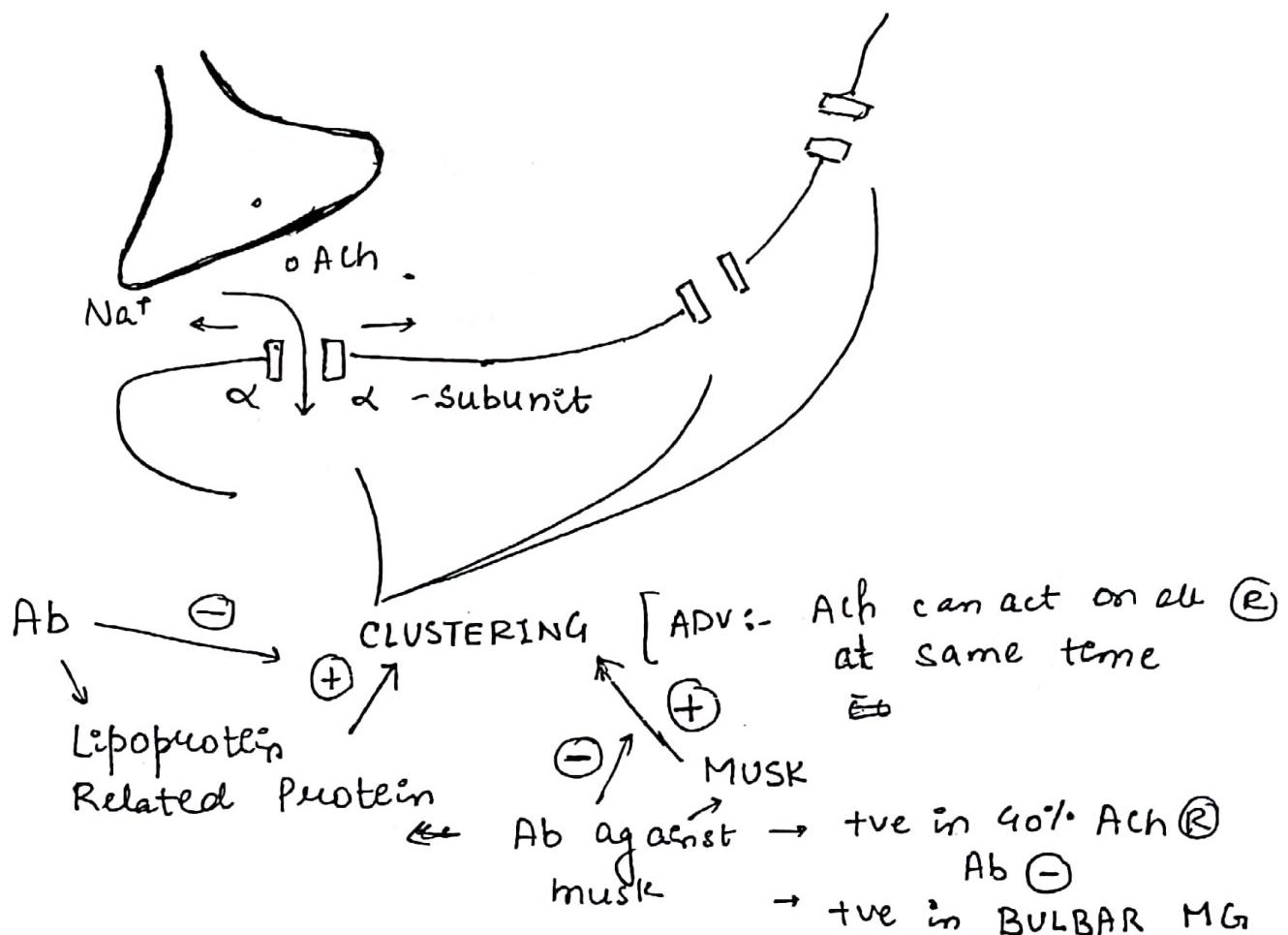
+ in 85% of pts. c gen. MG.

→ 50% [Ocular MG.] → [eye symptoms x 3 years]

-ve doesn't rule out MG.

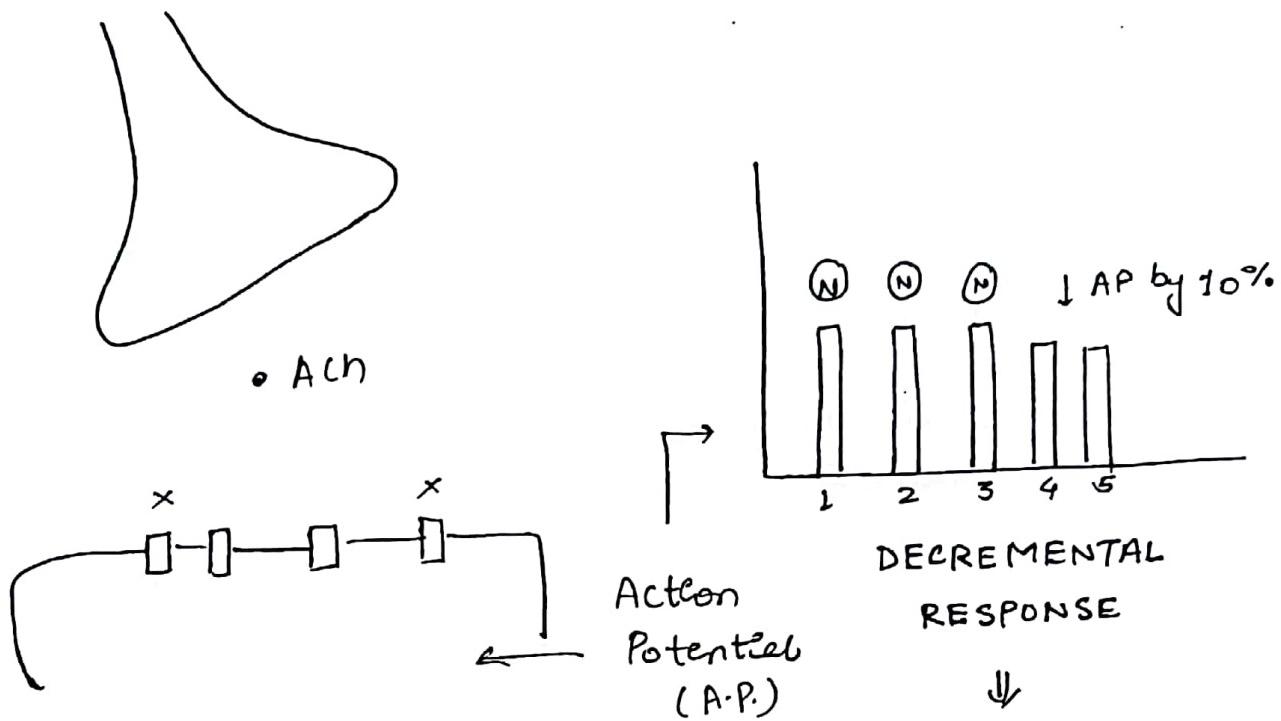
## 3) MUSCLE SPECIFIC TYROSINE KINASE (MUSK)

MUSK Antibodies



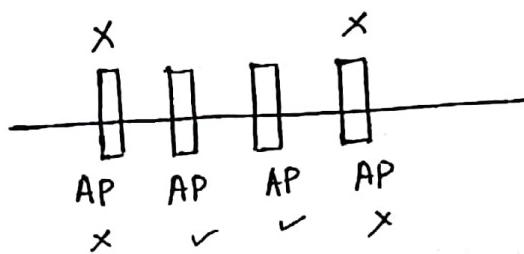
## 47 RAPID / REPEATED NERVE STIMULATION (RNS)

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5> SINGLE FIBRE EMG (SFEMG) S/o MG.

↑  
MOST SENSITIVE TEST  
CONFIRMATORY  
GOLD STD. TEST.



Difference in AP.  $\Rightarrow$  JITTER ↑↑.

Shows myopathic pattern

doesn't record jitter well.

BEST

SFEMG > EDROPHONIUM > RNS

**RX**

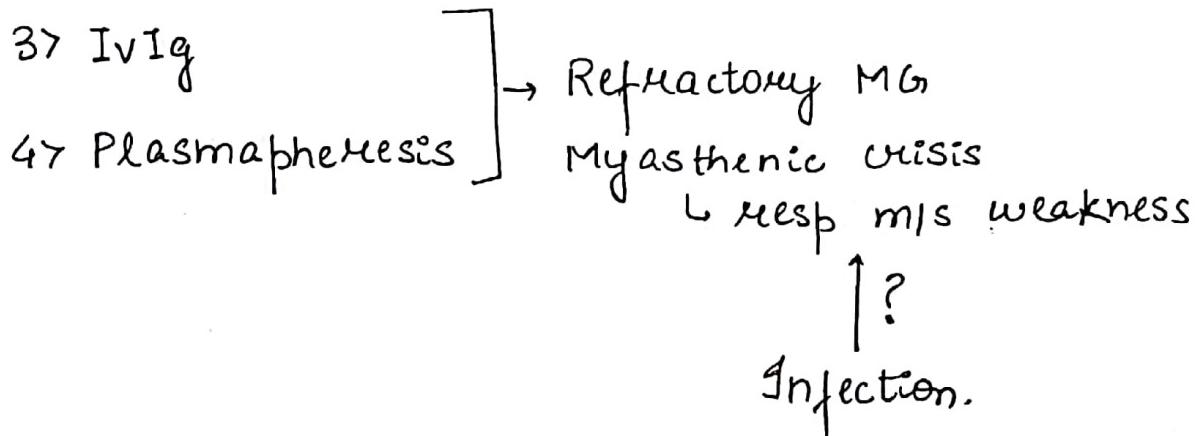
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1> ACh E  $\ominus$

| <u>PYRIDOSTIGMINE</u> |       | <u>NEOSTIGMINE</u>               |
|-----------------------|-------|----------------------------------|
| DOC                   | Ach ↑ | Ach ↑↑↑                          |
| Oncal                 |       | cholinergic crisis<br>Injectable |

2> IMMUNOSUPPRESANTS

MYCOPHENOLATE MOFETIL (MMF) — Best



5> THYMECTOMY

35% MG  $\rightarrow$  Drug Free

85% MG  $\rightarrow$  Symptom Remission

It is Recommended Inspite of medical control. (15-55yr) [MUSK Ab  $\ominus$ ]

**MOST USEFUL**  $\rightarrow$  In Thymoma pts.  
 ↳ local effect  
 ↳ Paraneoplastic synd.

NOT USEFUL IN

<15 yrs



Immuno Def.

>55 yrs

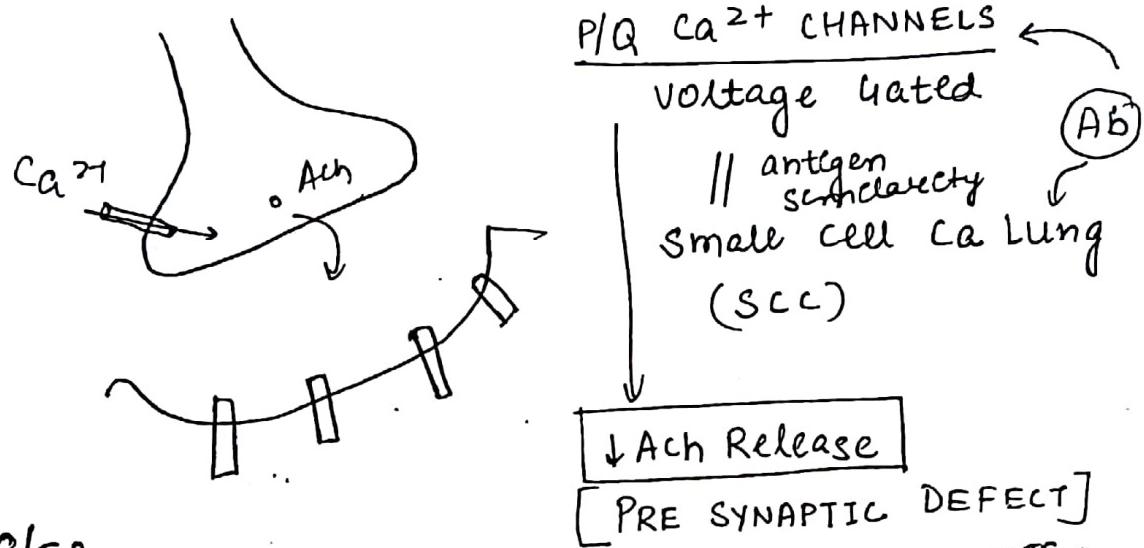


Vestigial

- Ocular MG
- Risk surgery  $\gg$  Disease
- MUSK Ab  $\oplus$  [↓ Benefit]

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## LAMBERTEN [LEMS]      EATON MYASTHENIC SYNDROME [PARANEOPLASTIC SYNDROME]

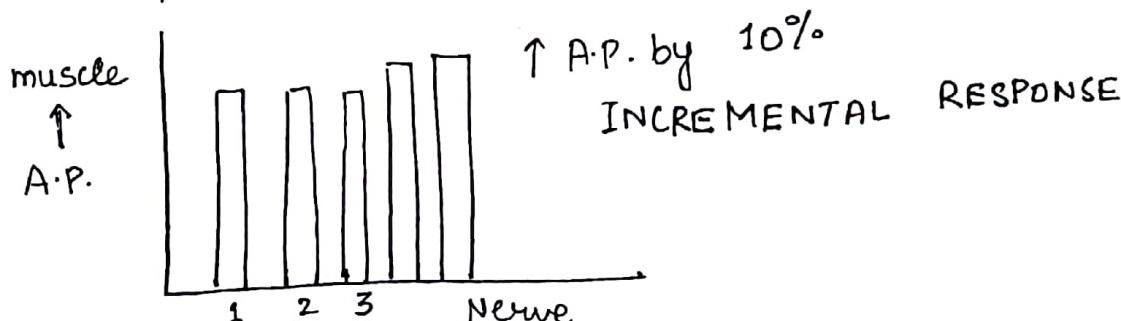


C/F :-

weakness skeletal  $>$  Facial  $>$  ocular [MG opp. seq.  
NOTE - ].  
DTR  $\downarrow / \ominus$  [MG, DTR N]  
Bladder involved [MG, Bladder N]

INV :-

- 1) Edrophonium +ve. (weakly +ve compared to MG)
- 2) Rapid N/V stimulation Test



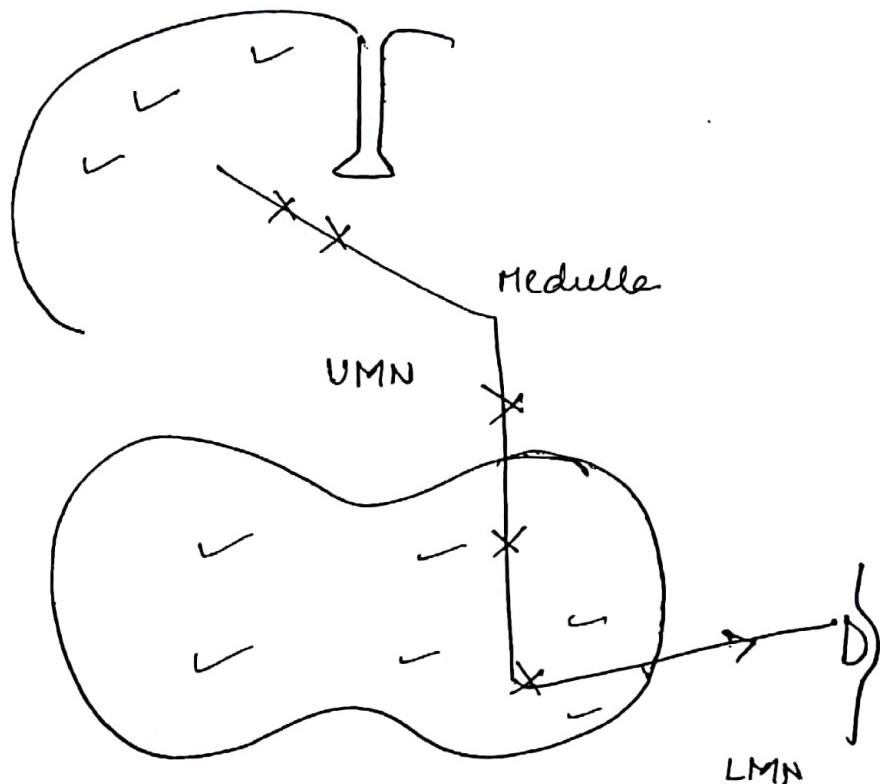
Rx -

356

▷ 3, Diaminopyridine  $\leftarrow$  DOC

3DAP [Tach Release]

MOTOR      NEURON      DISEASE



### ① AMYOTROPHIC LATERAL SCLEROSIS (ALS)

cortico  $\leftarrow$  UMN = LMN  $\leftarrow$  due to AHC

spinal

Tract

weakness is starts distally.

Amyotrophic  $\Rightarrow$  no trophic factors  
weakness occurs.

② 1° LATERAL SCLEROSIS (PLS)

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Degeneration of CS Tract  $\Rightarrow$  UMN

③ SPINAL MUSCULAR ATROPHY

only LMN

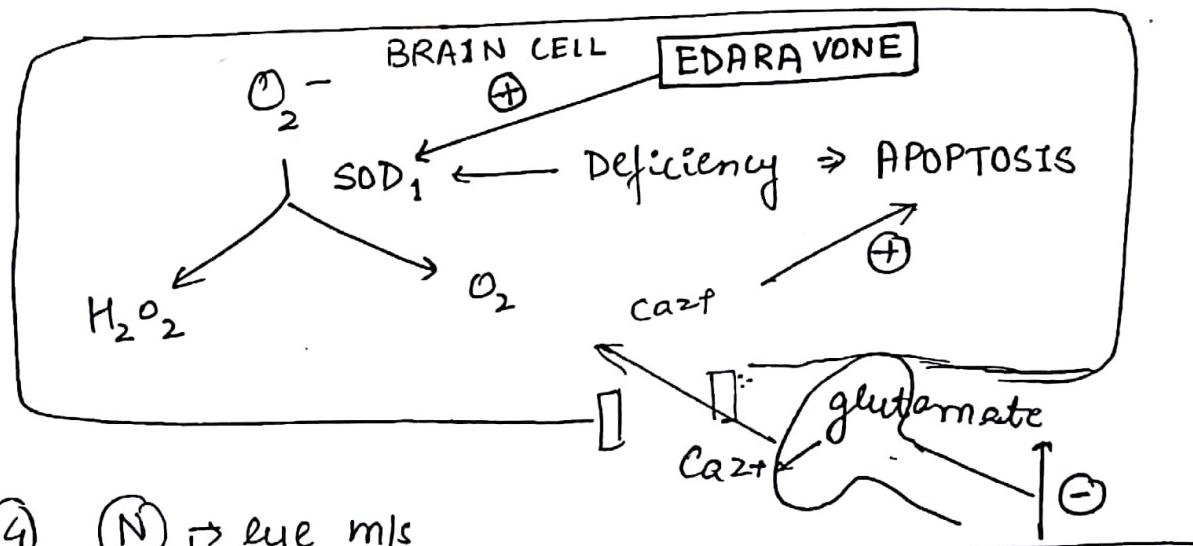
ALS

C/F -

1) Elderly

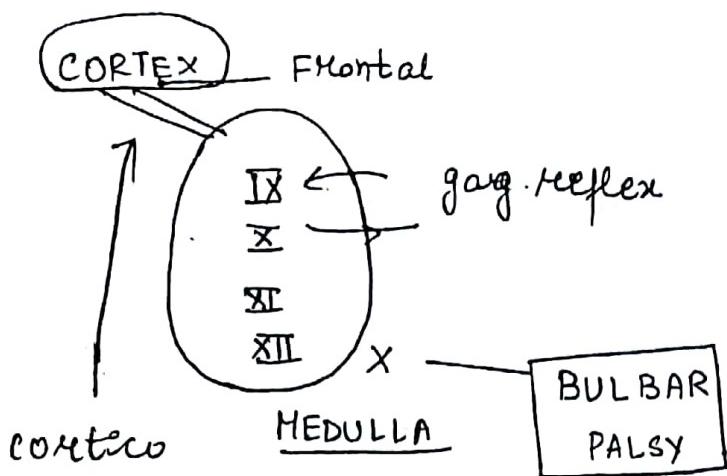
2) Fasciculations  $\leftarrow$  [PATHOGENOMIC]

3) SUPEROXIDE DISMUTASE (SOD1) Deficiency



- ④ N  $\rightarrow$  eye m/s  
sensory  
Bladder  
Cognition.

⑤



|               |    |
|---------------|----|
| Dysarthria    | +  |
| Dysphagia     | +  |
| Labile effect | +  |
| Gag Reflex    | ++ |

| BULBAR PALSY |                    |
|--------------|--------------------|
| ++           | ALS                |
| ++           | Polio              |
| ⊖            | M.G. [Bulbar M.G.] |

# ATAxia

DRG = DORSAL Root  
ganglion

|                                  | FREIDRICH<br>ATAxia                            | TABES<br>DORSALIS                          | SUBACUTE<br>COMBINED<br>DEGENERATION           |
|----------------------------------|------------------------------------------------|--------------------------------------------|------------------------------------------------|
| <u>TRACTS</u>                    | POST.<br><br>Pyr./c.s.<br><br>Spino cerebellar | POST.                                      | POST.<br><br>Pyr./c.s.<br><br>Peripheral n/vs  |
| <u>VIBRA-</u><br><u>TION</u>     | (-)                                            | (-)                                        | (-)                                            |
| <u>PROPIO-</u><br><u>CEPTION</u> |                                                |                                            |                                                |
| <u>PAIN, TEMP</u>                | (+)                                            | (+)                                        | (+)                                            |
| DTR.                             | (-) Early DRG involved                         | (+)                                        | (+) → (-)<br>neuropathy                        |
| Babinski                         | +ve                                            | (-)                                        | +ve                                            |
| ASSOCIATE<br>DT                  | cardiomyopathy<br>Optic Atrophy<br>DM.         | Syphilis<br>ARP (+)<br>Bladder disturbance | ↓ vit B <sub>12</sub><br>Megaloblastic anaemia |

FREIDRICH's

Tri-nucleotide Repeat sequence = GAA

- AR

- Chr. 9

TABES DORSALIS

Syphilis.

Argyll Robertson Pupil.

Bladder Disturbance

SACB

↓ Vit B<sub>12</sub>.

↓  
Megabolastic  
Anaemia

CEREBELLAR LESIONS

Dysmetria → Past Pointing

Titubation → persistent head nodding

Intentional Tremor

Dysdiadochokinesia

Pendular knee jerk

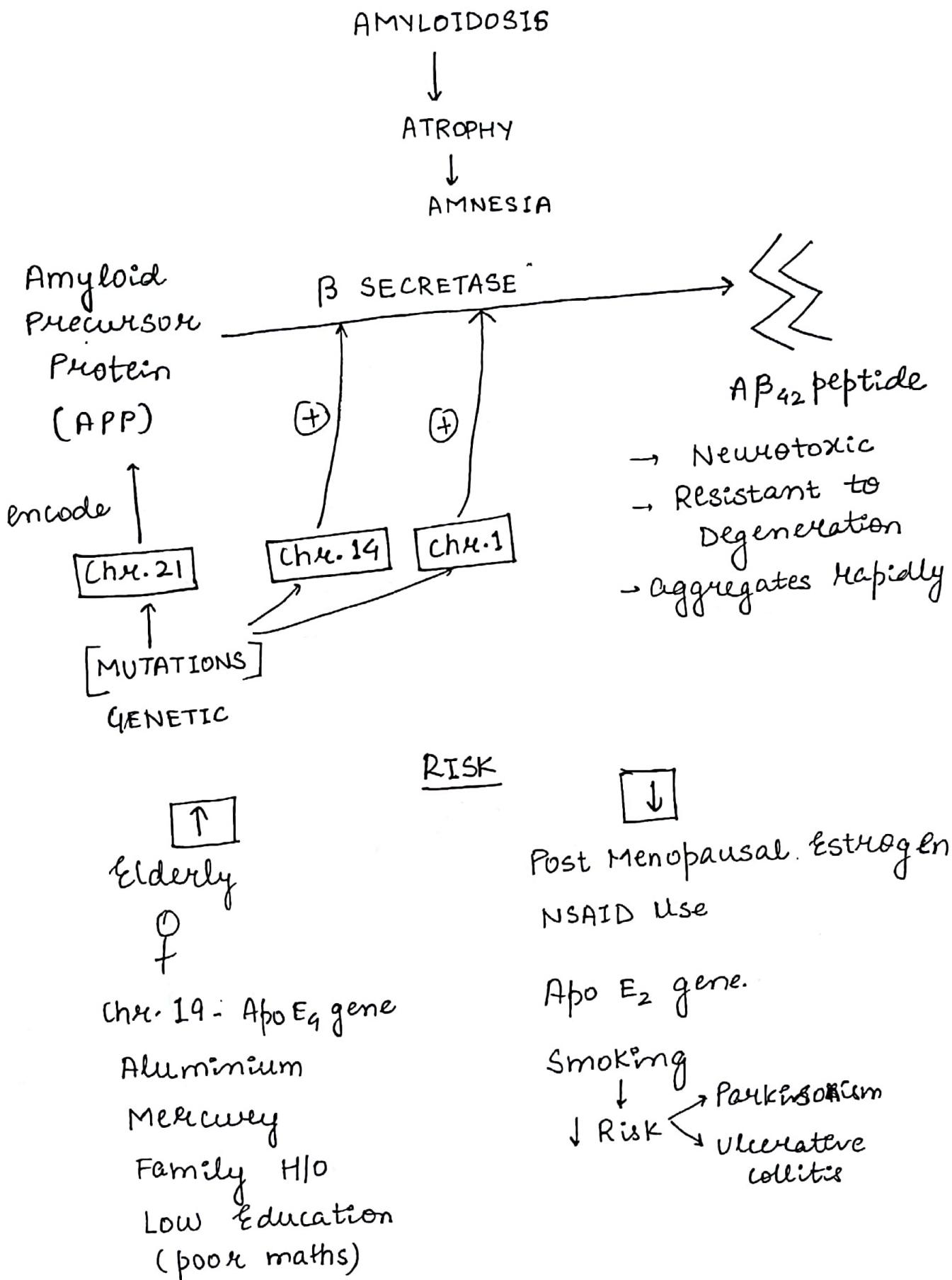
Romberg's Test (+) → Lesion in Post. column

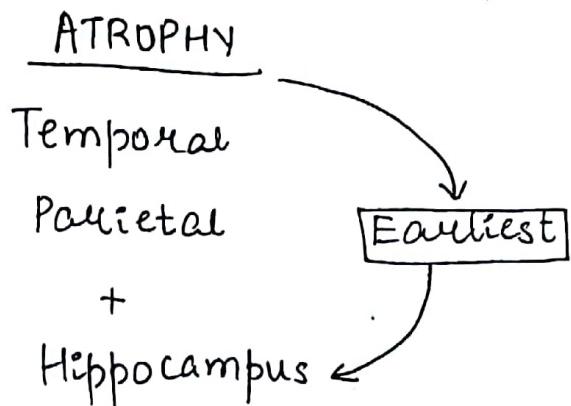
Broad Based gait

Tendency to fall towards lesion.

# ALZHEIMER DISEASE

361



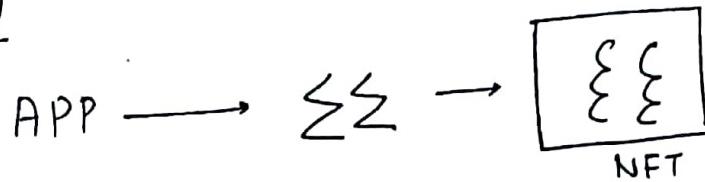
C/F

- 
- ↓ Ach.
- ACALCULIA  
is not seen.  
[DSM CRITERIA]
  - AGNOSIA  
not seen in early onset  
Alzheimer's (age < 65yrs)  
[ICD CRITERIA]
  - DELUSION → Doctor replaced by enemy  
(false belief)  
" OF DOUBLES
- TROPHY

MNESIA (anterograde)  
PHASIA (Anomia)  
NOSOGNOSIA (unaware)  
PRAXIA  
GNOSIA (can't identify)  
NOSMIA  
SPIRATION PNEUMONIA (cause of death)
- CAPGRAS  
syndrome  
(in 10% of pts)

## BIOPSY

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### 1) NEUROFIBRILLARY TRIANGLES

Intracellular

Correlate  $\cong$  severity

[TAU] - Hyper  $\text{PO}_4^-$  microtubular protein  
s/o neurodegeneration

Also seen in TAU Pathies

### 1) Fronto Temporal Dementia

- Behavioural Ab<sup>(N)</sup> due to frontal lobe involvement
  - early
  - severe
- memory loss
  - late
  - mild
- Age of onset < 65 yrs.
- insight  $\ominus$

### 2) Progressive Subcortical Gliosis (PSP)

- extended posture
- downward gaze  $\ominus$  fall
- dementia

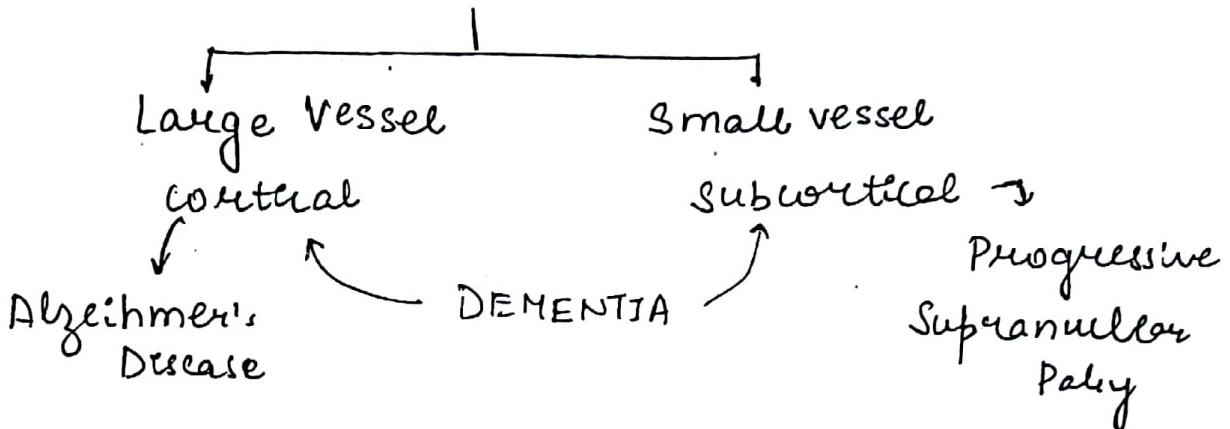
### 3) Corticobasilar Degeneration [PD + myoclonus + Dystonia]

## 27 SENILE NEURITIC PLAQUES (SNP)

364

- extracellular
- correlate  $\propto$  Age

## CEREBRAL AMYLOID ANGIOPATHY (CAA)



## 3) GRANULOVASCULAR DEGENERATION

Best seen in HIPPOCAMPUS

## HUNTINGTON'S CHOREA

- Huntington gene ] Trinucleotide Repeat Sequence  
[Chromosome 4 - short arm] defect  
 $\text{CAG} > 40$  repeats.
- AD inheritance
  - 2 successive generations are affected
  - 1 Parent affected  
[chance 50%] 1:2
  - If Both parents affected.  
[chance 75%] (3:4)

ANTICIPATION

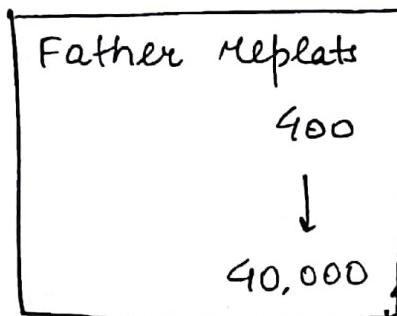
(11-soys)  $\hookrightarrow O^+$  = early onset 2nd Decade  
 (Father)  
 Mother = Late Onset 4<sup>th</sup> Decade.

LENGTHENING

Larger Defect

$\rightarrow \uparrow$  severe

$\rightarrow$  early onset (from father)



Mother Repeats

400

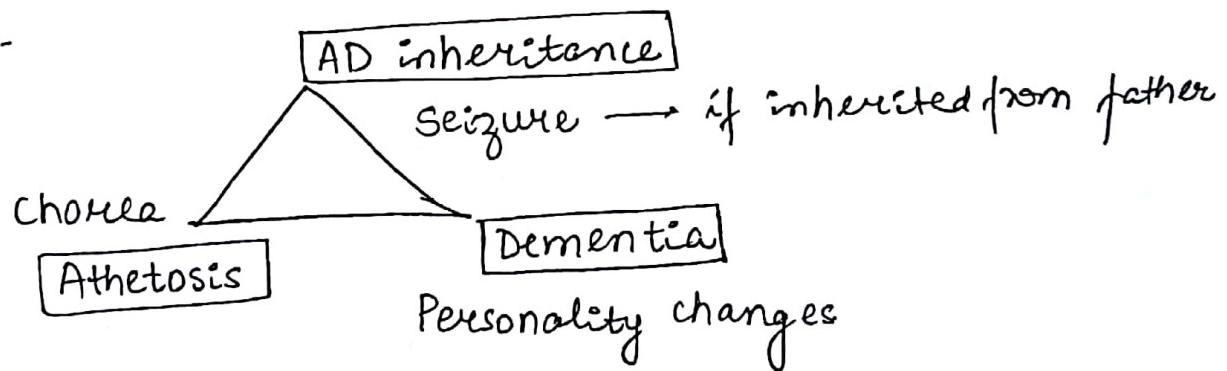


400

anticipation

↳ occurs due to lengthening.

C/F -



ATROPHY → in CAUDATE NUCLEUS.

$\downarrow$  Ach  $\downarrow$  GABA Intra striatal  
 $\uparrow$  DA

Rx  $\rightarrow$  DA  $\ominus$   $\rightarrow$  Haloperidol

DA Depletor  $\rightarrow$  Tetrabenazine  $\leftarrow$  DOC

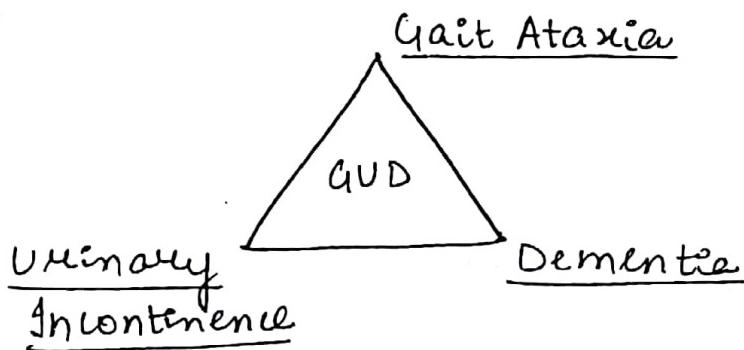
## NORMAL PRESSURE HYDROCEPHALUS (NBB)

CSF PRESSURE →  $N = 50 - 150$

$$\hookrightarrow NPH = \boxed{150 - 180}$$

↓ CSF Absorption. ← SAH  
↑ Meningitis

C/F



### MAGNETIC GAIT

- external hip rotation
- shorter strides
- low ground clearance..

SCISSORING GAIT → Spastic CP

CHARLIE CHAPLIN GAIT → Tibial Torsion

Rx

V-P shunt



1st / Most responsive symptom to improve on VP shunt  
ATAxia

## QQ WERNICKE'S ENCEPHALOPATHY

367

■ PREDISPOSED -

1) Hyperemesis

2) Alcohol Intake

B<sub>1</sub> ~~#~~ Deficiency

CO-FACTOR for.

$\alpha$ -Keto glutarate dehydrogenase  
Pyruvate Dehydrogenase

GLUCOSE ACCUMULATION

Mitochondrial Damage

NEUROTOXIC

C/F

GLOBAL confusion

GOA

ophthalmoplegia

Ataxia

Rx

THIAMINE REPLACEMENT X 14 Days.  
(100 mg/day)

1st Improve = ophthalmoplegia

[Glucose Infusion can Precipitate it]

# KORSAKOFF'S PSYCHOSIS / ALCOHOL DEMENTIA

368

DEMENTIA → CONFABULATION

False story to hide  
memory loss

## SITES

Perequeductal Grey Matter

Mamillary Bodies

Holamus → [AMNESTIC DEFECT]

## CONFUSIONAL STATE

- 1) seizure
- 2) T.I.A.
- 3) Metabolic → ↓ glucose  
↓ alcohol

## TRANSIENT GLOBAL AMNESTIA

Both anterograde + Retrograde amnesia

## CNS INFECTIONS

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### BACTERIAL / PYOGENIC MENINGITIS

M/C/C

Adolescent / Adult = N. MENINGITIDIS  
(epidemic)

Elderly = STEPTO. PNEUMONIA  
(Community acquired)

CSF

Ⓐ appearance  
N

PYOGENIC

|                 |               |                         |
|-----------------|---------------|-------------------------|
| Appearance      | Transparent   | Turbid                  |
| cell count      | $\leq 5$      | Pleocytosis (N $\gg$ L) |
| Protein         | 15-45 mg/dL   | ↑↑                      |
| Glucose         | 40-70 mg/dL   | ↓↓↓                     |
| Cl <sup>-</sup> | 116-126 meq/L | ↓ / N                   |

Hypoglycorrhexia = ↓ CSF Glucose

Rx

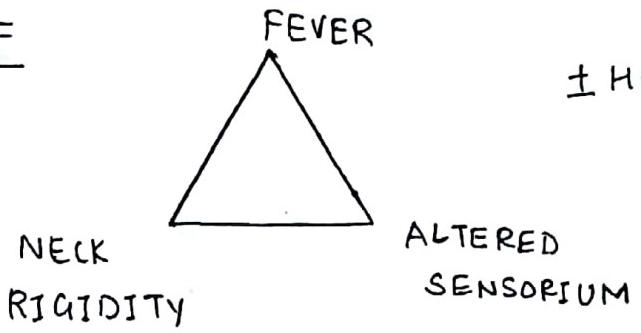
N. MENINGITIDES → Ceftriaxone  $\times$  7 Days

S. PNEUMONIAE → Ceftriaxone + vancomycin ]  $\times$  14 Days

>60yrs ↓

LISTERIA → Ampicillin

C/F



± HEADACHE.

370

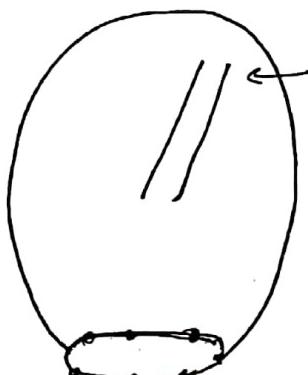
Dexamethasone

10 ~~mg~~ mg IV Stat

↓  
1st Dose of antibiotic

TBM

M/c Meningitis In India



Endarteritis

↓ Infarct

TBM ATT x 1 month  
↓ sensorium

① ATT induced hepatitis

↳ hepato, encephalo  
pathy

② ↑ ICT →  
cerebral salt  
wasting

③ Infarct

④ Tuberculoma

⑤ Hydrocephalus

Hydrocephalus

Basal Exudates → Tuberculoma

Reactivation

CSF



→ COB-WEB

→ Pleocytosis [L >> N]

→ Protein ↑↑↑

→ Glucose ↓ Cl- ↓↓↓

GOLD STD TEST = Culture of CSF

Rx

ATT x 12-18 months (↓ Reactivation)

Steroids x 2 months [⊖ Endarteritis]

## VIRAL ENCEPHALITIS

371

MICC → ENTEROVIRUS

→ epidemic = ARBOVIRUS

→ sporadic = HSV type 1

## HSV ENCEPHALITIS



CSF

→ xanthochromia

SAH

→ CT scan.

(CSF) N

xanthochromia

→ Traumatic LP

→ Pleocytosis

→ ↑ Protein

→ (N) Glucose

→ Cl<sup>-</sup> ↓

MOST SENSITIVE TEST = PCR FOR HSV IN CSF

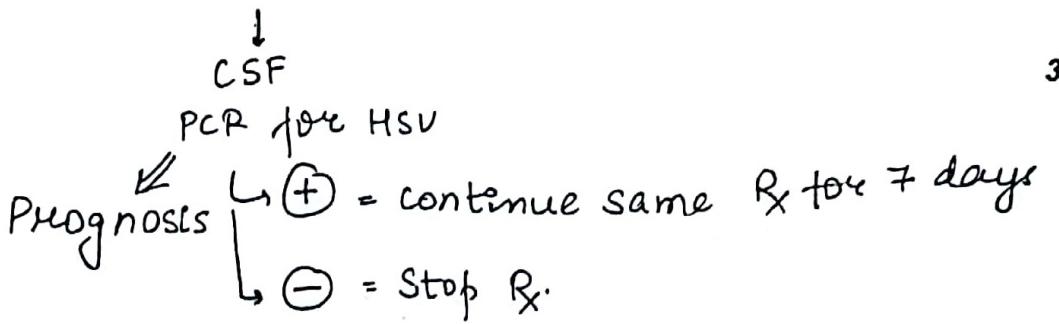
MRI

Bitemporal hyperintensities

|       | T <sub>1</sub> | T <sub>2</sub> |
|-------|----------------|----------------|
| Brain | ↑              | ↓              |
| CSF   | ↓              | ↑              |

Rx Acyclovir - 10mg/kg IV q8hly × 14 days





## PROGRESSIVE MULTIFOCAL LEUCOENCEPHALOPATHY (PML)

Jc Virus → Oligodendrocytes  
Inclusion bodies

A/c -

Immunocompromised host

↳ HIV + (80%, m/c host)

Transplant Recipient

C/F - Visual field Defects. (M/c)

Inv

MRI → Hyperintensities

↓ Demyelination

↓ CSF (PCR for Jc virus)

↓ Brain Biopsy

Rx

not available

Prognosis Death 3-6 months of onset

## PRION DISEASE

373

CREUTZFELD JACKOB DISEASE (CJD)

DNA/ RNA -

Transmittable →  
dural Grafts  
corneal Grafts

C/F -

Dementia + myoclonus (M/L)

Inv

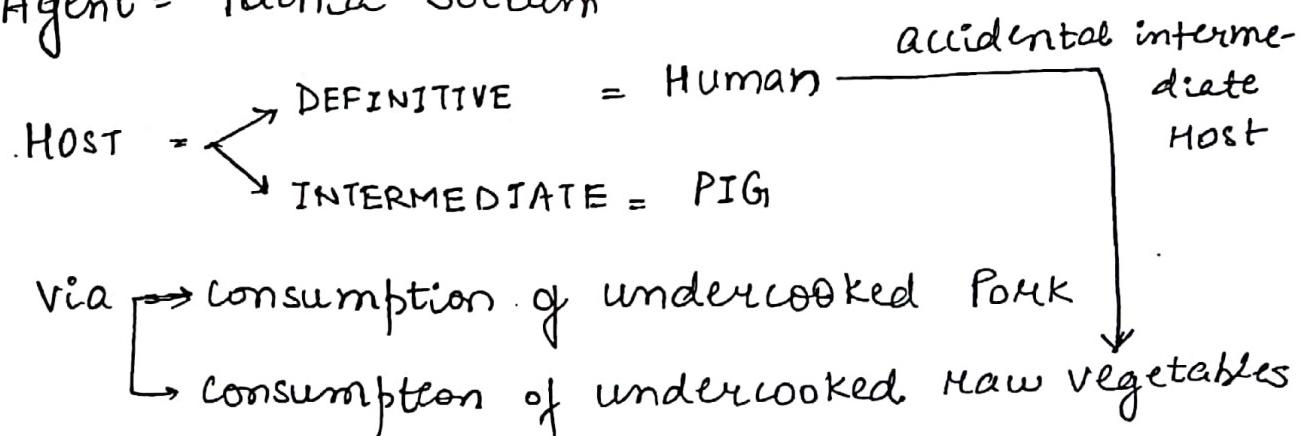
EEG - Biphasic waves

Brain Biopsy - spongeform degeneration

Rx - not available

## NCC [Neurocysticercosis]

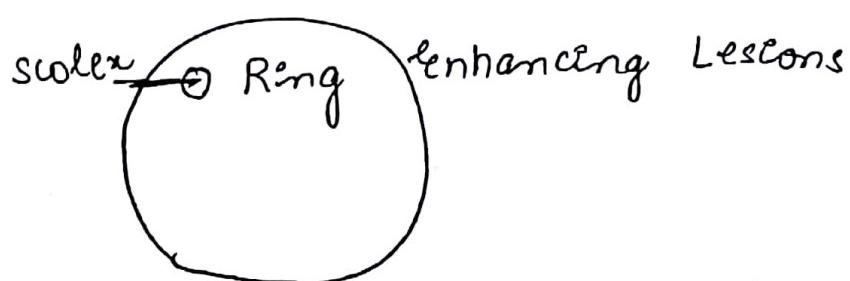
Agent = Taenia Solium



C/F - Seizure (M/L)

Inv -

CE → CT  
MRI



## STAGES

374

|           |        |
|-----------|--------|
| (viable)  | Oedema |
| VESICULAR | +      |
| (Dying)   |        |
| COLLOIDAL | +++    |
| (Dead)    |        |
| CALCIFIED | -      |

Rx

## ANTI-PARASITIC

**DOC** → ALBENDAZOLE      PRAZIQUENTAL

$\downarrow$   
15 mg/kg/day  $\times$  8-28 days

+ Steroids + A.E.D. x 6 months

↓  
CT Scan

↓  
calcified

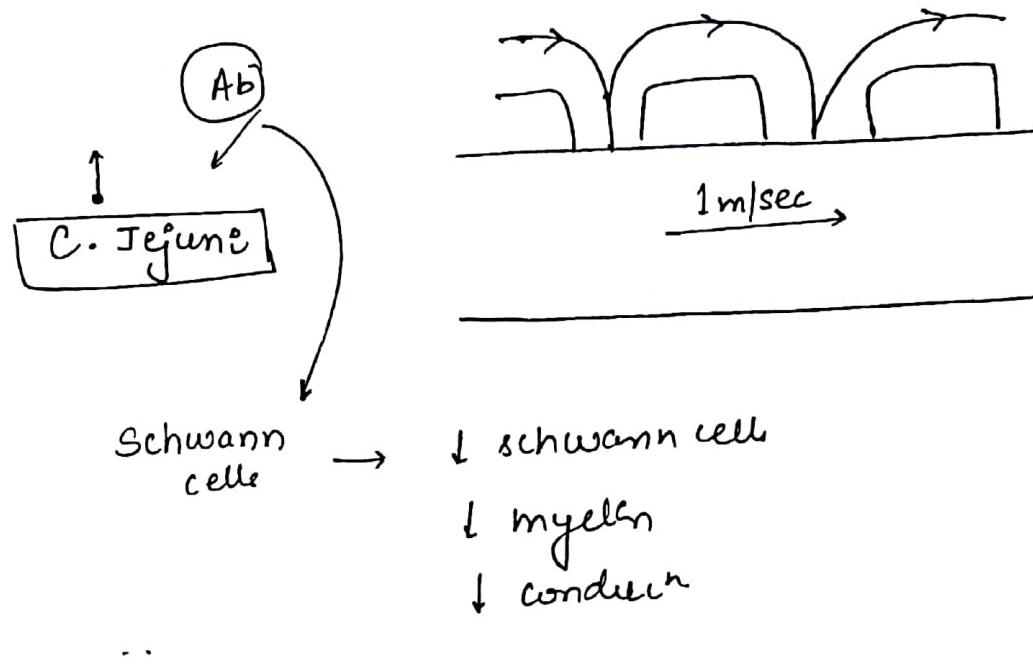
Taper 2-3 months

↓  
STOP.

| <u>↓ OTHER</u>                                                                                                                                               | <u>TYPES OF CIBS</u>                                                                                                                           |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------|
| <div style="border: 1px solid black; padding: 5px; display: inline-block;">AIDP</div><br><4wk<br>Motoric<br>Sensory<br>>90% children<br>mostly<br>GM, Ab +ve | <div style="border: 1px solid black; padding: 5px; display: inline-block;">AMAN</div><br>motoric<br>only<br>children<br>young adult<br>GD & Ab |
|                                                                                                                                                              | <div style="border: 1px solid black; padding: 5px; display: inline-block;">AMSAN</div><br>M = S<br><br>mostly<br>adult<br><br>worst Prog.      |
| <div style="border: 1px solid black; padding: 5px; display: inline-block;">CIDP</div><br>>9wk.                                                               |                                                                                                                                                |

# GUILIAN BARRE SYNDROME

375



- Post infectious
- Demyelinating
- Poly neuropathy

VACCINES causing GBS :-

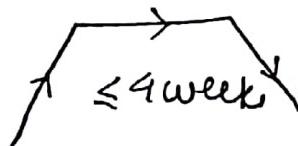
RABIES (neural)

Influenza

C/F

ASHBURY CRITERIA

→ Ascending Paralysis → Symmetrical  
Distal → Proximal  $\leq 4$  weeks



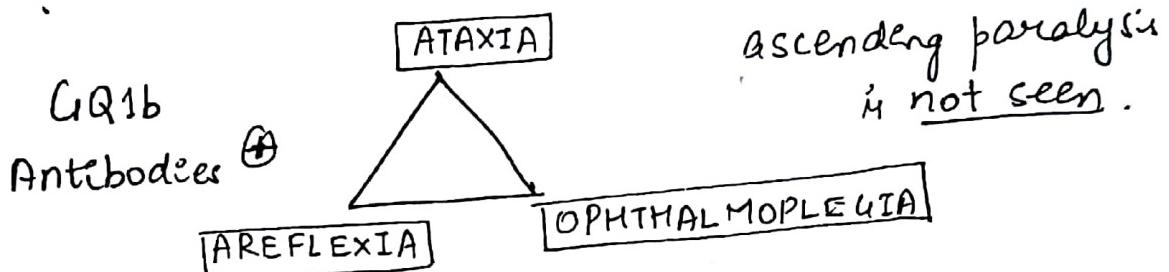
Areflexia  
Minor sensory  
Bladder - spared

M/c: cranial N/V involved  
= VII<sup>th</sup> (B/L, LMN)

ACUTE      B INFLAMMATORY      DEMYELINATING      POLYNEUROPATHY  
(AIDP)

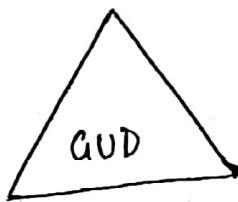
### VARIANT OF GBS

#### MILLER FISCHER VARIANT / SYNDROME



#### MILLER FISCHER TEST $\leftarrow$ (DNB)

Done in Normal pressure Hydrocephalus  
CSF Drained (30mL)



$\downarrow$   
cognition  
 $\downarrow$   
improved  
 $\swarrow$   
then go for  
V-P-Shunting

### Inv for GBS

- 1) Nerve Condu<sup>n</sup> Study
  - $\downarrow$  N/V condu<sup>n</sup> velocity
  - $\downarrow$  A.P.

## ⇒ CSF

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↑ Albumin      ] Albumino cytological  
No pleomorphism      ] Dissociation.

RX

- 1) IV Ig  
~~200g~~ 2g m/kg over 50 days.] → Both are equally effective
- 2) Plasmapheresis      Best in 1st 14 Days

Steroids is not recommended

## PROGNOSIS

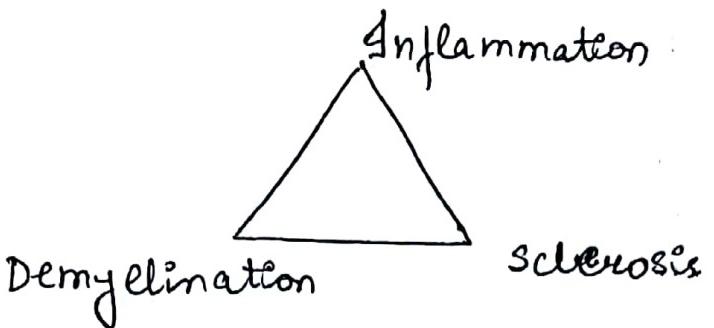
Recovery occurs in 85% [IV Ig & Plasmapheresis will not alter the sequelae]  
Sequelae → 10%

Death → 5%

|                    | INFLAMMATORY     |               | MYOPATHY | INCLUSION BODY MYOSITIS |
|--------------------|------------------|---------------|----------|-------------------------|
|                    | DERMATO MYOSITIS | POLY MYOSITIS |          |                         |
| AGE                | Any              | >20 yrs       |          | >50 yrs                 |
| MUSCLE INVOL.      | Proximal         | Proximal      |          | Distal                  |
| SKIN Changes       | +                | -             |          | -                       |
| Ass. to malignancy | +(15%)           | -             |          | -                       |
| EYE                | (N)              | (N)           |          | (N)                     |
|                    | (Mus. kinase ↑↑) | ↑↑            |          | ↑↑                      |

## MULTIPLE SCLEROSIS

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DISSEMINATED

→ Time  
→ Space.

C/F

## 1) SENSORY

## 1st HIC Symptom

↑ exposure to HEAT  $\Rightarrow$  UTHOFF SIGN

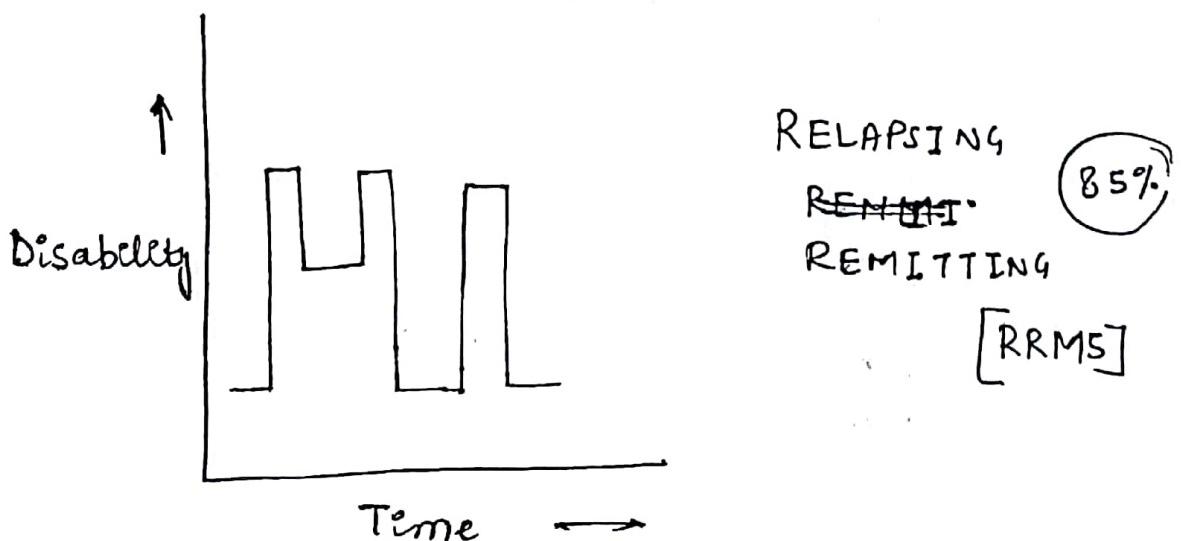
## ICE PACK TEST

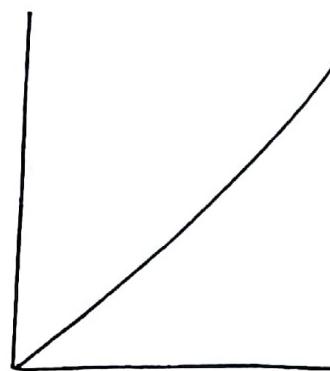
Cold ⊖ AChE ⇒ In MG pts.  
Weakness ↓

## ② OPTIC NEURITIS

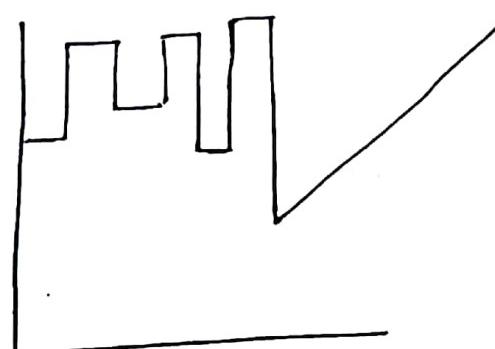
### ③ SPASTICITY

## TYPES

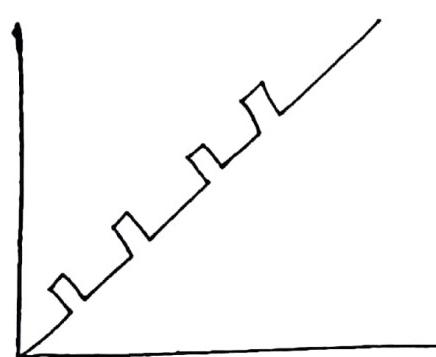




1° PROGRESSIVE MS (PPMS) 15%



2° PROGRESSIVE MS (SPMS)



PROGRESSIVE RELAPSING MS (PRMS)

### STAGING

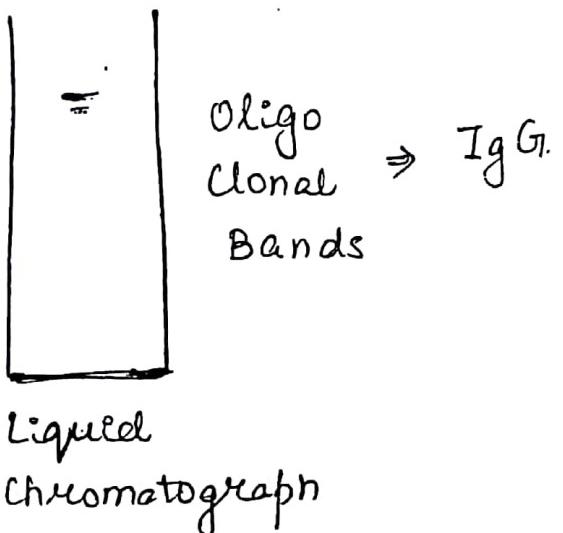
MS = EXTENDED DISABILITY SCORING SCALE (EDSS)

SAH = HUNT & HESS SCALE

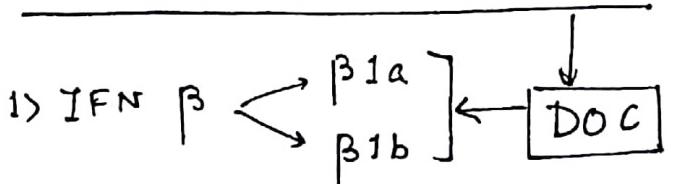
MG = OSSERMAN GRADING

INVMAC DONALD CRITERIA

MRI → Demyelination  
 ↓  
 Plaque ] → Periventricular

CSFRxACUTE ATTACK

METHYL PREDNISOLONE (DOC)

DISEASE MODIFYING AGENTS

2) Glatiramer

3) FingoLimo [ORAL]

4) Natalizumab [BEST] → S/E = PMLE

## D/D of DESCENDING PARALYSIS

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Botulism

Polio, Porphyria

Diphtheria



# ENDOCRINE

- Dr. Achin



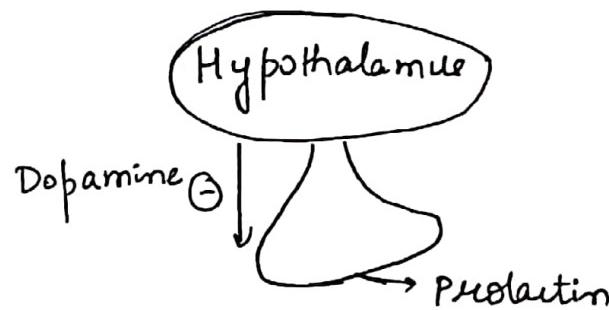
## PROLACTIN

Secreted in Ant Pituitary

Prolactin making cell LACTOTROPH

FUNC:-

- 1> Induce & maintain the process of lactation
  - 2> prolactin hormone  $\xrightarrow{(-)}$  GnRH  $\rightarrow$  LH  $\downarrow$   $\hookrightarrow$  ovulation
- ↓
- sexual drive  $\leftarrow$  ↓ Testosterone  $\hookrightarrow$   $\ominus$  menstruation
- ↓
- Spermato genesis



## HYPEPROLACTINEMIA

### ETIOLOGY -

#### A) PHYSIOLOGICAL

1> Lactation

2> ♀

$\uparrow$  Estrogen  $\xrightarrow{+}$  ↑ PRL

3> Sleep [NREM sleep]

4> Chest wall stimulation

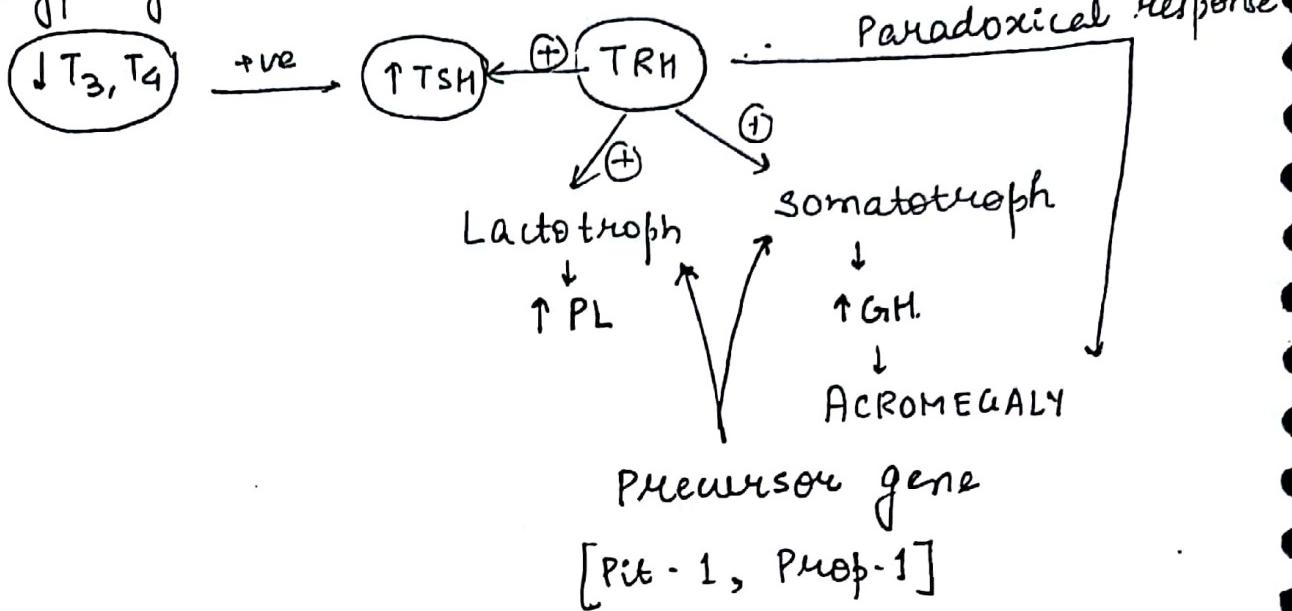
→ nipple stimulation

→ chest trauma or surgery

→ herpetic Lesions

## S&B SYSTEMIC DISORDERS

### 1) Hypothyroidism



### 2) CKD

→ ↓ excretion of prolactin



### 3) SEIZURE

Post Ictal (30 mins)

### C) DRUGS (Iatrogenic)

#### Dopamine $\ominus$

→ Typical Antipsychotics

- ↳ Haloperidol
- ↳ CPZ

→ Atypical Antipsychotics

- ↳ Risperidone

→ Metoclopramide

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### Dopamine Depleters

CH<sub>3</sub> Dopa

Reserpine

CCB - verapamil

### H<sub>2</sub> ANTAGONIST

Ranitidine

Cimetidine

⇒ These drugs cause hyperprolactinemia due to blockage of Infundibular Pathway

### D) PITUITARY ADENOMA

PROLACTINOMA → M/c type

<10mm

MICRO (90%)

F:M = 20:1

>10mm

MACRO (10%)

F:M = 1:1.

C/F → ♀ → Galactorrhea - 80%  
↳ B/L.



Amenorrhea

↑ PL → ↓ LH

↓ Ovulation

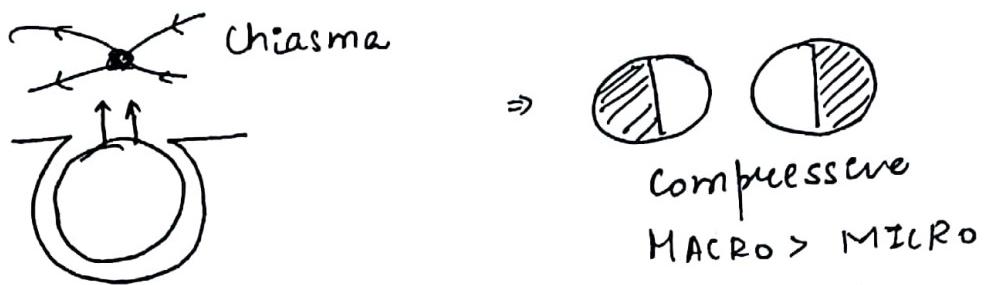
↓ Estrogen

↓ Osteoporosis

Inferility (M/c presentation)

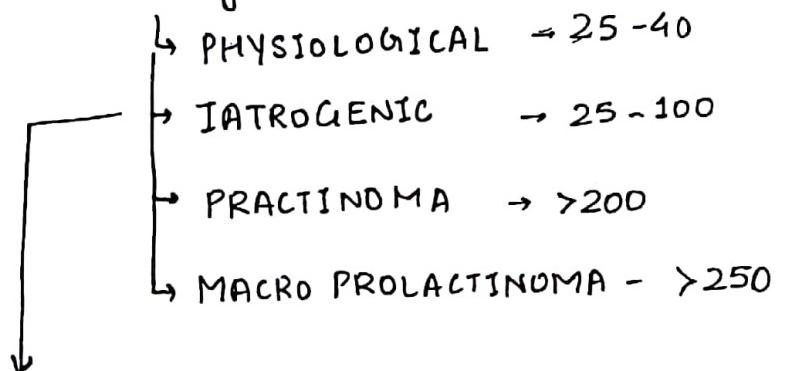
$\sigma^{\rightarrow} \rightarrow \downarrow$  Libido  
 Azoospermia  
 Infertility

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### S. PROLACTIN

$$(N) = 5 - 25 \mu\text{gm/l}$$



Stop offending drug  
 Reassess PL after 72 hours

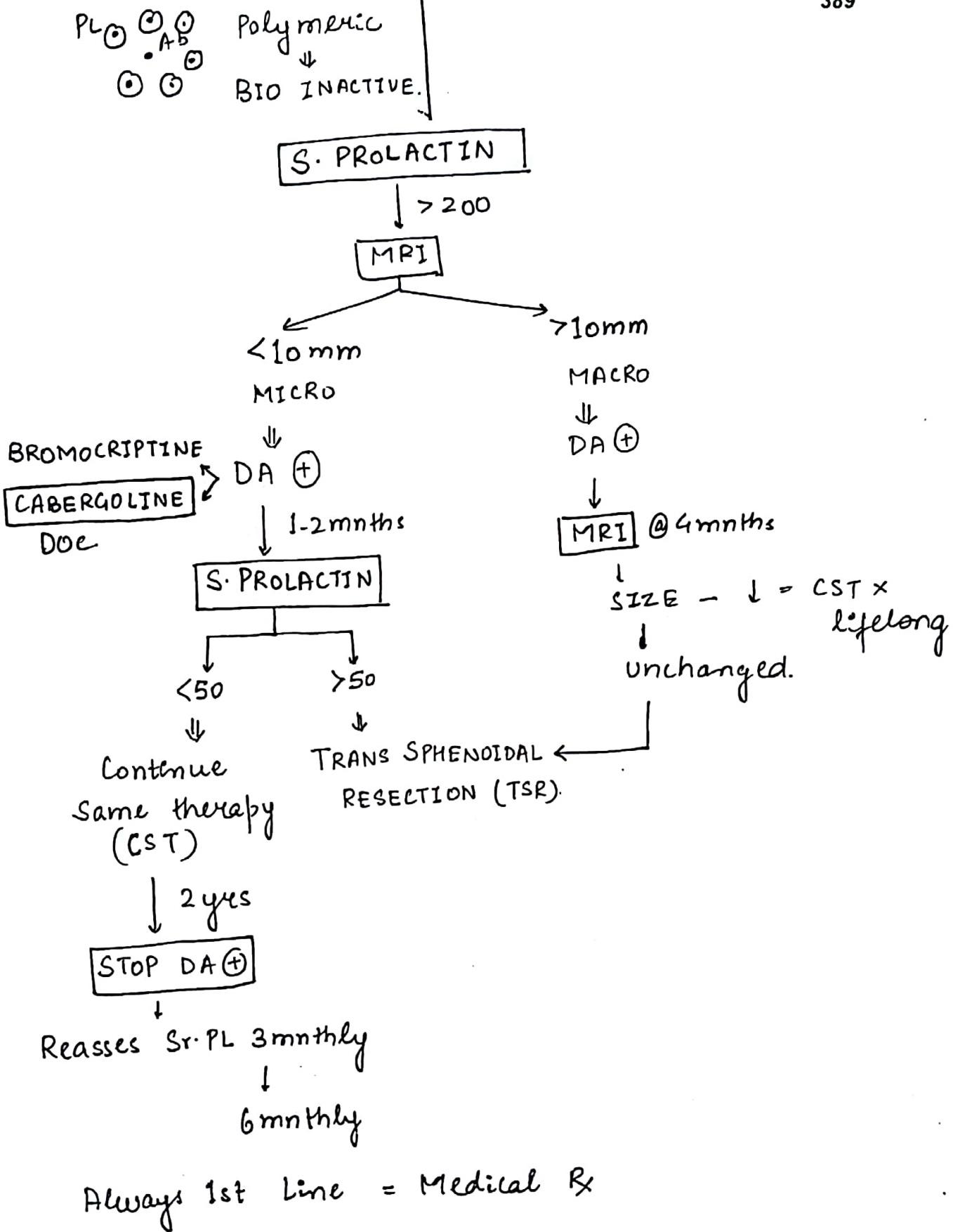
### MACROPROLACTIN

Symptoms -  
 Prolactinoma -  
S. Prolactin ↑↑  
 [FALSE HIGH]

PROLACTIN = Peptide hormone  
 (198 A.A)  
 ↳ 85% monomeric

### HOOK EFFECT

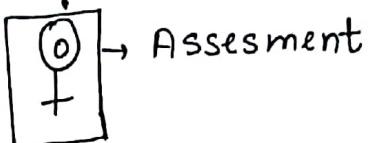
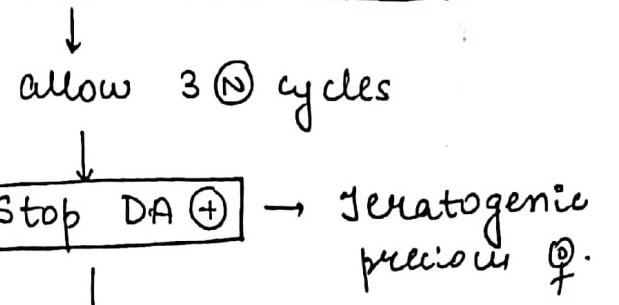
Symptoms +  
 Prolactinoma +  
S. Prolactin (N)  
 [FALSE (N)]



Always 1st Line = Medical Rx

PROLACTINOMA ON DA + WANTS TO CONCEIVE

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Rare < [Headache] DA +  
[BROMOCRIPTINE]  
↓ Vision | no response  
[SURGERY] (TSR)

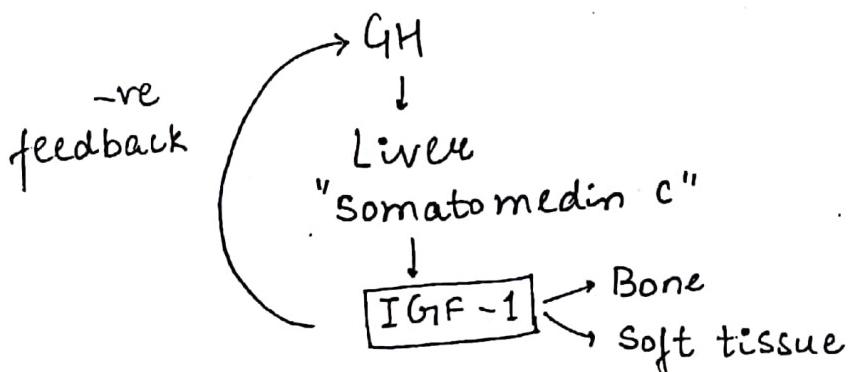
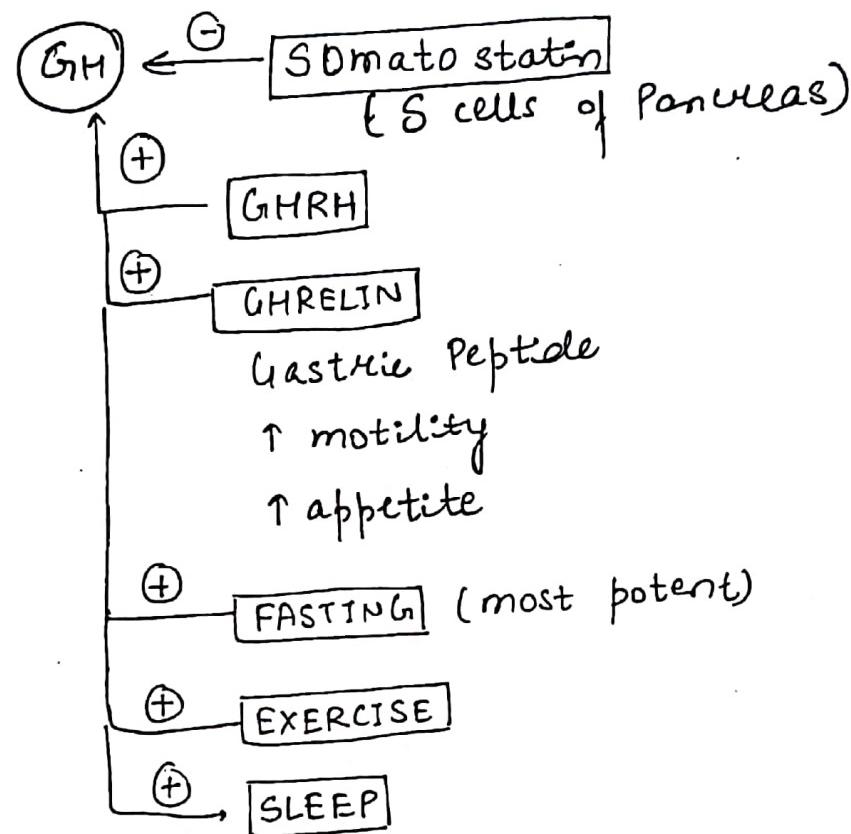
Prolactinoma in ♀ are asymptomatic

DOC for Prolactoma = CABERGOLINE  
↓  
In ♀  
Long acting  
Convenient intake  
↓ nausea  
Better effect  
BROMOCRIPTINE  
FERTILE ♀ → BROMOCRIPTINE

## GROWTH HORMONE

391

- Released from Ant. Pituitary
- By SOMATOTROPHS (Most abundant cells) 50%
  - Lactotrophs > Gonadotrophs  
(20 - 30%)
  - Gonadotrophs  
(10 - 20%)



GH

CARBOHYDRATE

Diabetogenic

PROTEIN

ANABOLIC

IGF-1

392

Anti-diabetic

FAT

LIPOLYTIC

ANTI-LIPOLYTIC

GH  $\xrightarrow{(+)}$  Lipase  $\rightarrow \uparrow \text{FFA}$

↓  
Insulin

Resistance

↓  
Diabetogenic

$\uparrow \text{GH}$

↳ epiphyseal fusion.

↳ BEFORE = GIGANTISM

↳ AFTER = ACROMEGALY

ACROMEGALY

ETIOLOGY

$\uparrow \text{GH}$

$\uparrow \text{GHRH}$

PITUITARY

↳ Somatotrophic  
Adenoma (M/c)  
↓

Loss of feedback

→ MAMMO SOMATOTROPHIC

ADENOMA  $\rightarrow \uparrow \text{PL}$

$\uparrow \text{GH}$

HYPOTHALAMUS

HAMARTOMA

ECTOPIC

BRONCHIAL CARCINOMA

## ECTOPIC

ISLET CELL CA of PANCREAS

393

C/F

CVS → LVH

Diastolic Dysfunc<sup>n</sup>

HTN

CAD

M/CC of DEATH  
ACUTE MI.

Resp → Nasal turbinate Hypertrophy  
obstructive sleep apnoea (OSA)

GIT → ↑ Liver + spleen (Hepatosplenomegaly)

Q Colonic Polyps >> cancer  
Benign

ENDOCRINE → DM (Insulin resistance)  
Goitre

SKELETAL → Tall stature  
Large digits  
Prognathism

Jaw malocclusion

[↑ space bet<sup>n</sup> lower incisors]

Fleshy nose.

## INVESTIGATION

394

- 1) GH ASSAY → not useful test

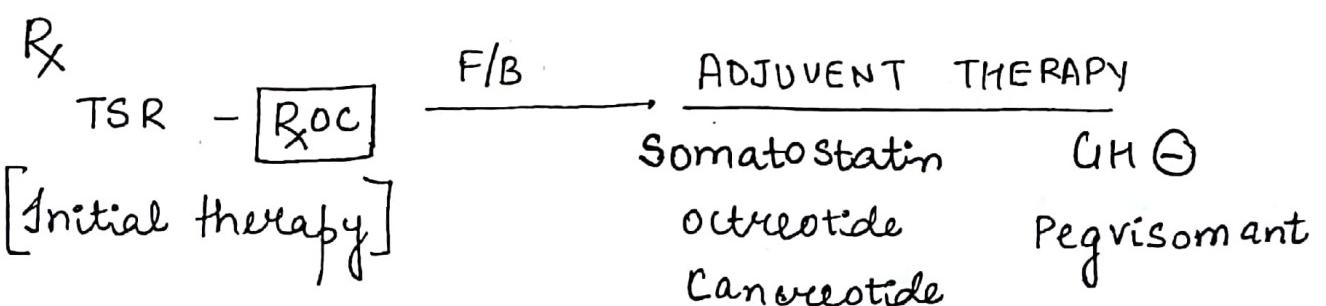
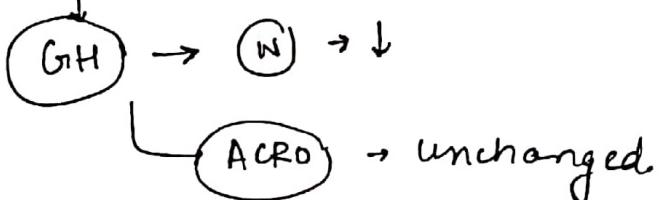


- 2) IGF-1 ASSAY  
Best screening Test

- 3) GH SUPPRESSION TEST → confirmatory Test

$$[GH \propto \frac{1}{\text{glucose}}]$$

75 gm glucose (oral)



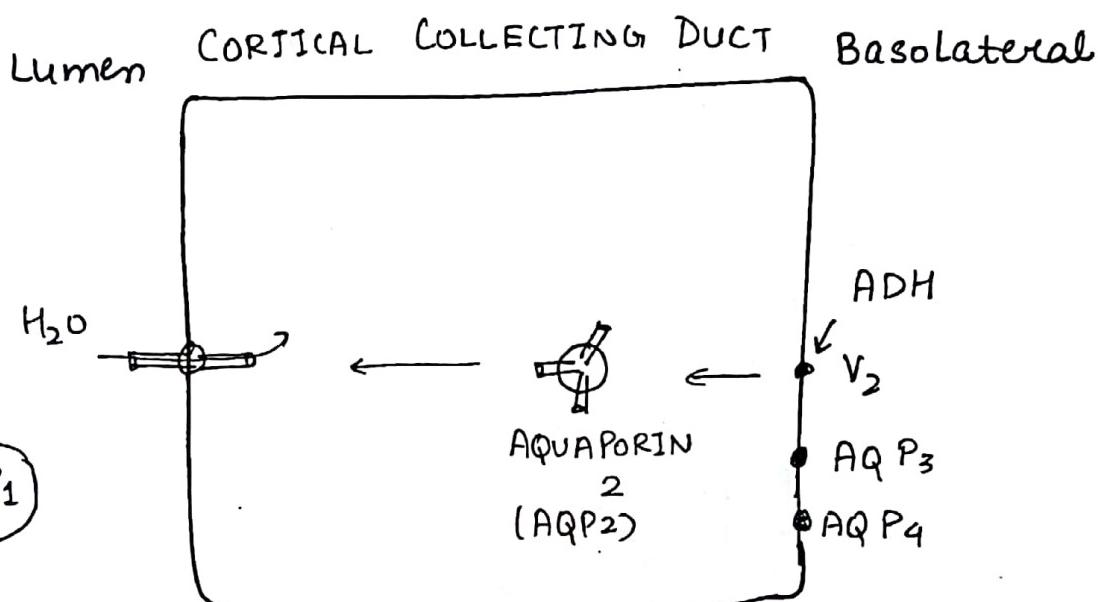
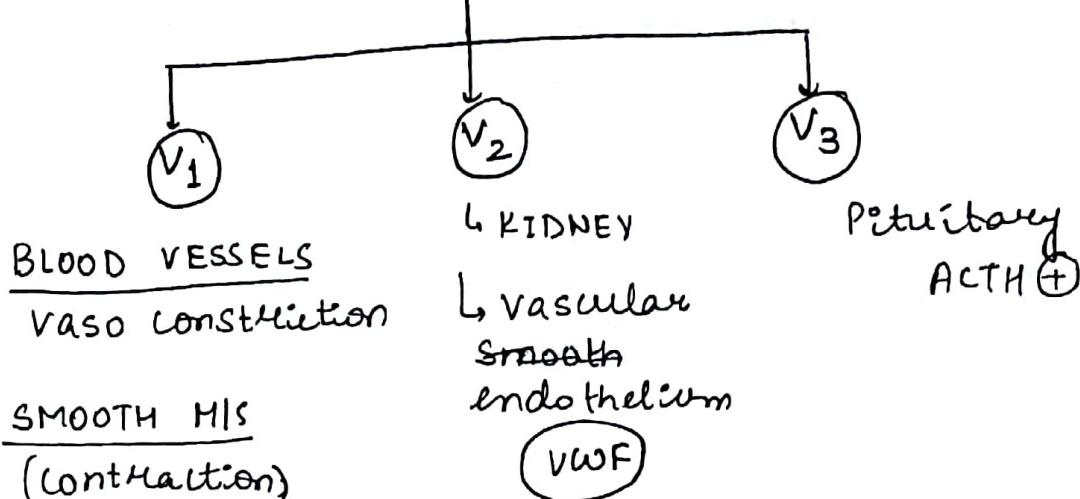
### INSULIN STIMULATION TEST

$GH \propto \frac{1}{\text{glucose}}$  → on giving Insulin.  
glucose ↓ → GH ↑ (N)

Dwayfum → GH unchanged

## ADH / VASO PRESSIN

395



AQP<sub>1</sub>  
↓  
PCT ← ADH  
Independent

### (N) values

S. Osmolarity = 275 - 295 mosm/L

U<sub>H2O</sub>ne osmolarity = 300 - 1000 mosm/L

St. Na<sup>+</sup>

135 - 145 meq/L

St. K<sup>+</sup>

3.5 - 5 meq/L

## POLYURIA

396

>50ml/kg/day

>3L/day



↑ Solute = ↓ H<sub>2</sub>O

Isosmolar

### SOLUTE/OSMOTIC DIURESIS

Glucose

↓  
Urine osmolality

Mannitol

>300 (N)

Ca<sup>2+</sup>

### DILUTE

H<sub>2</sub>O > Solute

U<sub>ur.</sub> osm < 300

→ DI

→ Psychogenic Polydypsia (PP)

H<sub>2</sub>O Deprivation Test

U<sub>re</sub>- osm. → (↑) = P.P.

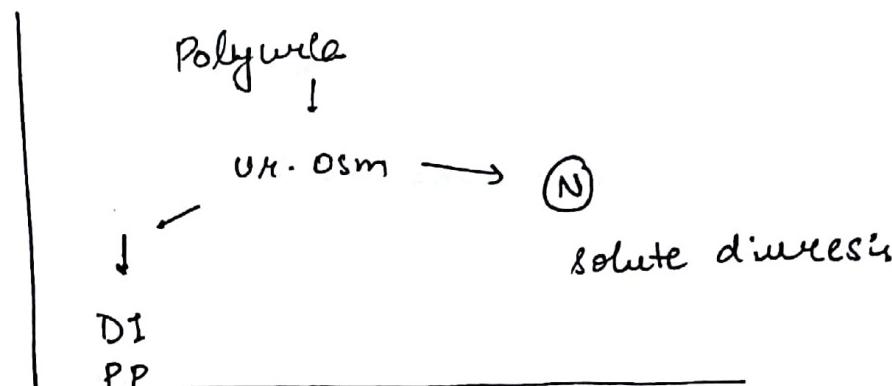
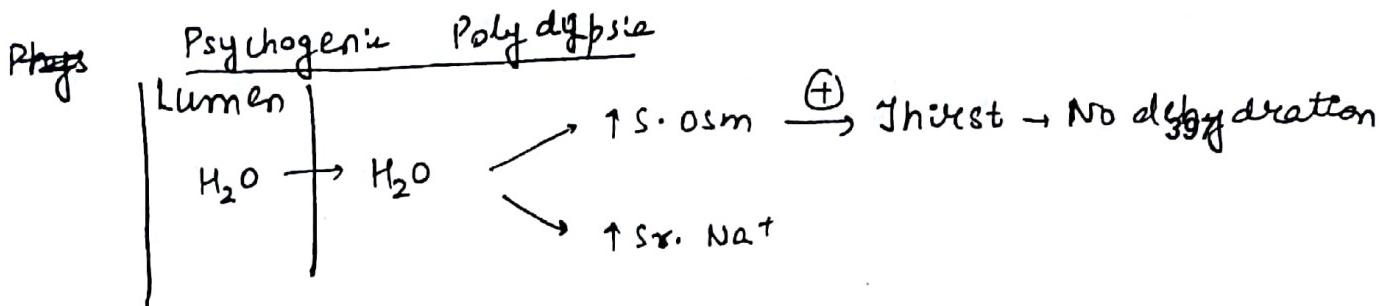
↳ unchanged = D.I.

ADH Stimulation Test

U<sub>re</sub>. Osm → (↑) = ADH Def."

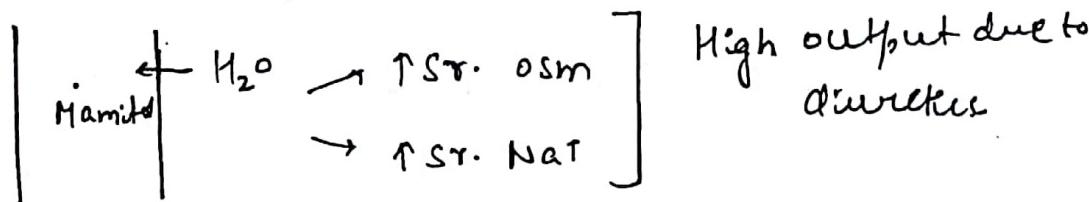
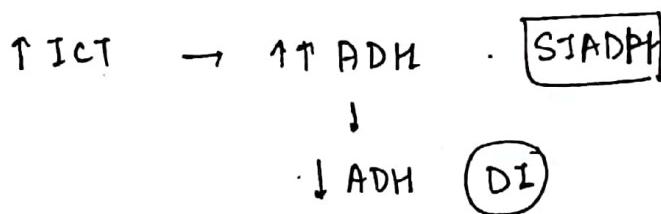
↳ unchanged = ADH Resistance

nephrogenic DI



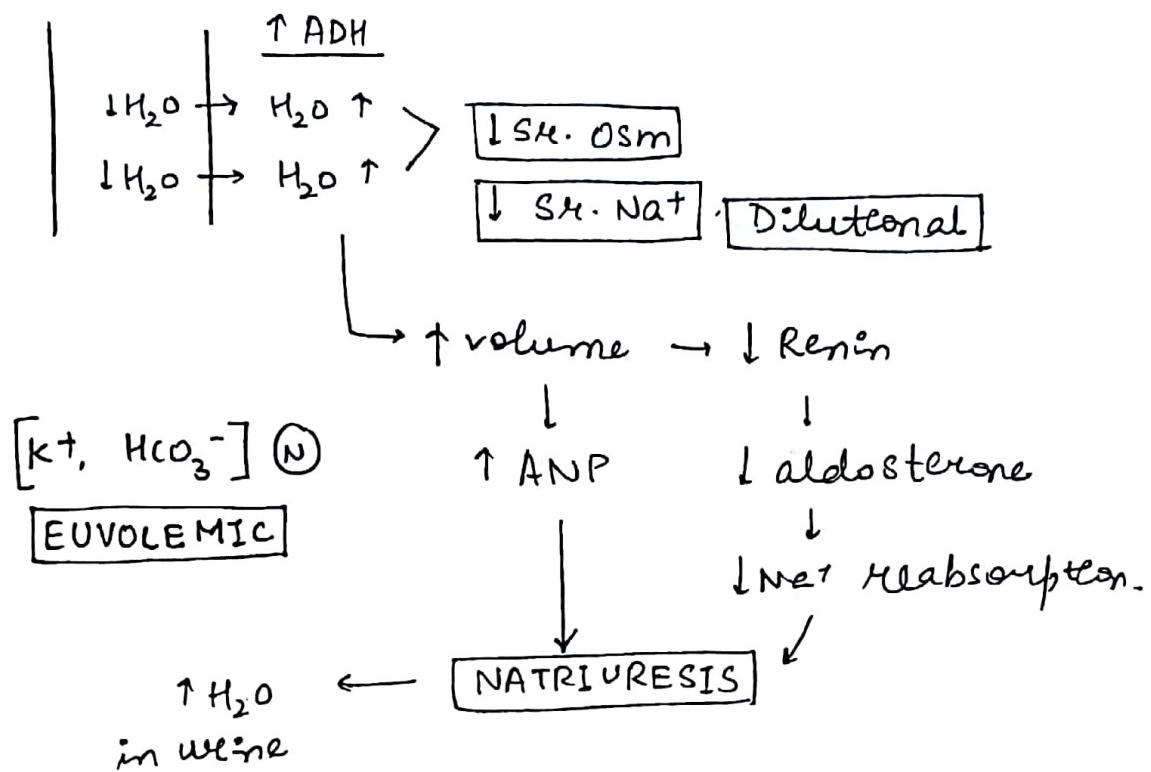
26

| CEREBRAL                                                                                                                                                              | SALT | WASTING | DISEASE                              |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|---------|--------------------------------------|
| $\uparrow \text{ICT} \rightarrow \text{BNP}$<br>$\downarrow$<br>$\downarrow \text{Na}^+, \downarrow H_2O$<br>$\downarrow$<br>Hyponatremia — Hypovolemia<br>natremesis |      |         | $\uparrow H_2O$<br>$\downarrow Na^+$ |



# SIADH [Syndrome of Inappropriate ADH]

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## HYPONATREMIA

### HYPOVOLMIC

Cerebral Salt  
Wasting Disease

### EUVOLEMIC

SIADH  
 $\downarrow$   
 **$H_2O$  Loading Test**

Pt. produce less  
urine than  $\textcircled{N}$  pt.

### HYPERVOLMIC

CCF  
CKD  
Chr Liver Disease

$$Rx = H_2O \text{ restriction Rx}$$

ADH  $\ominus \Rightarrow$  DEMECLOCYCLINE  
 $\downarrow$   
 VAPTAN (DOc)

$\boxed{\text{Na}^+}$

399

$\boxed{(\text{N})} = 135 - 145 \text{ meq/L}$

$> 120 = \text{Asymptomatic}$

$\boxed{110 - 120} = \text{GI symptoms}$   
↳ nausea

$\boxed{100 - 110} = \text{mild CNS symptoms}$   
giddiness  
Ataxia

Seizures →  $\boxed{< 100}$  cerebral edema

### PARATHYROID HORMONE

$\downarrow \text{Ca}^{2+} \rightarrow \uparrow \text{PTH}$

↳ Bone = Resorption

↳ Intestine = Absorption

↳ Kidney = Reabsorption

$\boxed{\uparrow \text{PTH}}$

④  $\boxed{2^\circ} \rightarrow \text{CKD}$

Vit D deficiency

Malabsorption.

$\boxed{1^\circ} \rightarrow \text{Parathyroid} \rightarrow \text{Hyperplasia}$

$\boxed{\text{Adenoma}} [\text{M/c/c}]$

M/c type = solitary

M/c site = Inf. Pth Lobule-

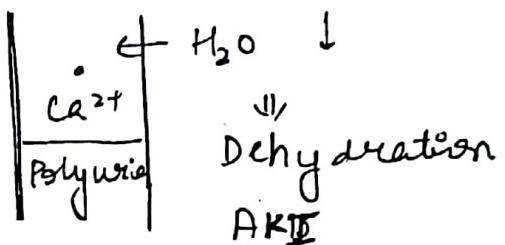
$3^\circ$  = PTH hyperplasia  $\rightarrow$  ADENOMA ( $3^\circ$ )  
 $2^\circ$        $1^\circ$

400

## HYPERCALCEMIA

C/F -

- nausea, vomiting
- constipation
- Bony pains (+)
- Renal calculi
- Abdominal Pain
- depression
- Psychosis



Rx -

1) Hydration.

2) Diuretics

Calcimimic  $\rightarrow$  Loop Diuretics

3) Bisphosphonates

(-) osteoclastic activity

DRONATES.

[Delayed onset of Action]

4> GALLIUM  
 5> PLICAMYCIN  $\rightarrow$  Osteoclast (-)

6> CALCITONIN

7> DIALYSIS

PSEUDO      HYPO      PTH

401

↓ Shr.  $\text{Ca}^{2+}$

↑ Sr. PTH

[PTH] Resistance

ALBRIGHT    HEREDITARY    OSTEODYSTROPHY (AHO)

Short stature

~~Round~~ Round Face

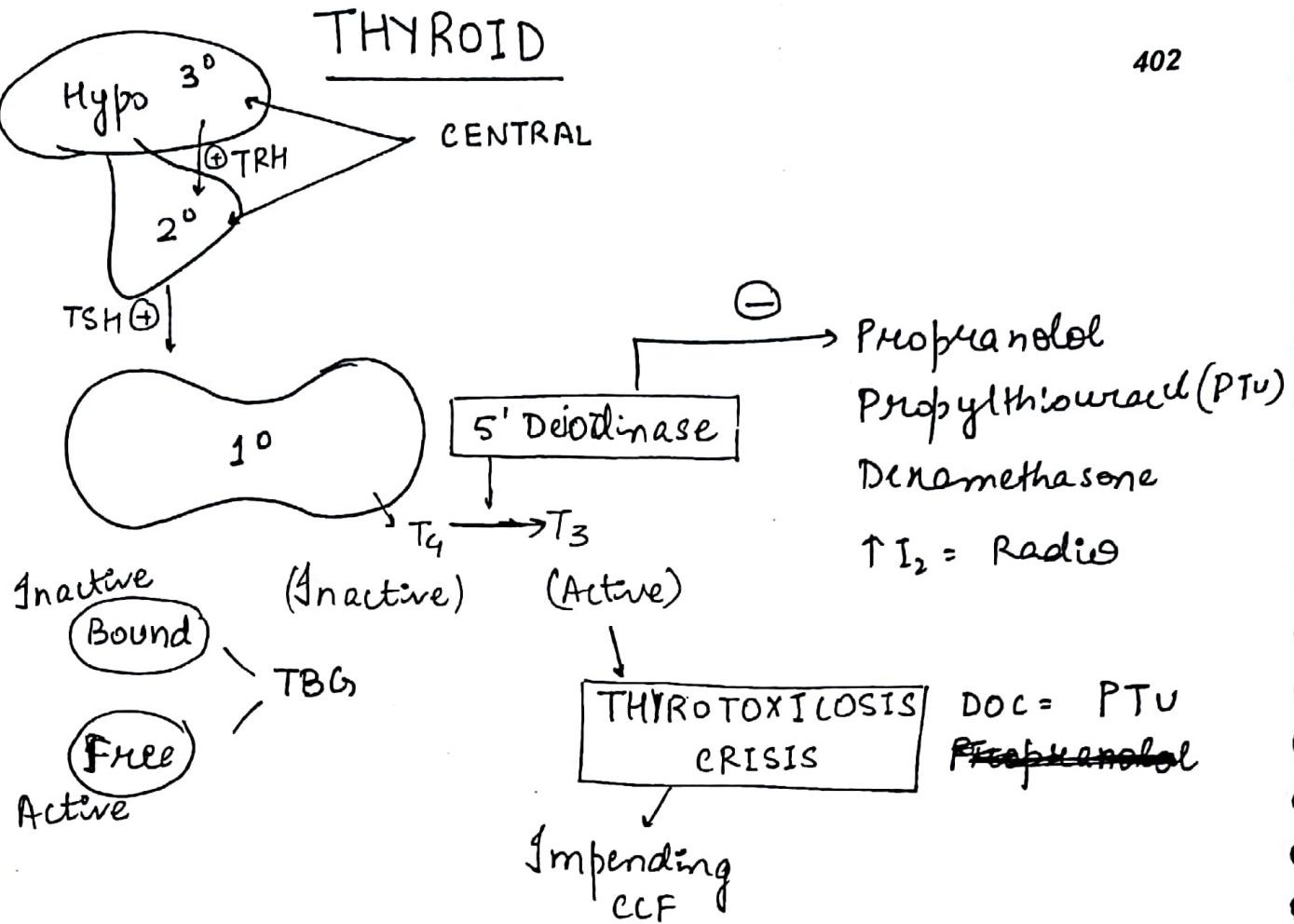
short 4<sup>th</sup>/5<sup>th</sup> metacarpal. (Brachydactyly)

PSEUDO      PSEUDO      HYPO      PTH

Shr.  $\text{Ca}^{2+} = \text{N}$

Sr. PTH = N

AHO Phenotype +



|                        | TSH          | FT <sub>3</sub>       | FT <sub>4</sub>       |
|------------------------|--------------|-----------------------|-----------------------|
| HYPOTHYR ( $1^\circ$ ) | $\uparrow$   | $\downarrow$          | $\downarrow$          |
| HYPERTHYR              | $\downarrow$ | $\uparrow$            | $\uparrow$            |
| 2° HYPOTHYR            | $\downarrow$ | $\downarrow$          | $\downarrow$          |
| SUBCLINICAL HYPOTHYR   | $\uparrow$   | Low $\textcircled{N}$ | Low $\textcircled{N}$ |

## HYPOTHYROID

Weight Gain  
Fatigue  
Cold Intolerance  
Constipation  
Menorrhagia

M/c Amenorrhoea

↓ H.R.

mild Diastolic HTN

Delayed Relaxation of  
Jerk  
[HUNG UP REFLEX]

Rx

## HYPOTHYROIDISM

L-Thyroxine  
[1.6 µg/kg/day]

↓ DOSE = elderly  
IHD

↓  
TSH after [6 weeks]  
[(N) = 0.35 - 5]

[Target = 0.35 - 2.5] → L-Thyroxine x Lifelong

|     |             |
|-----|-------------|
| TSH | L-Thyroxine |
| 10  | 75 µgm/day  |
| ↓   | ↓ +25       |
| 8   | 100 µgm/day |

## HYPERTHYROID

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Weight Loss  
Anxiety  
Heat Intolerance  
Diarrhoea  
Amenorrhoea

↑ H.R.

↑ S.B.P. / ↑ D.B.P.

Fine Tremors  
Exophthalmos

↓  
TSH 6 monthly

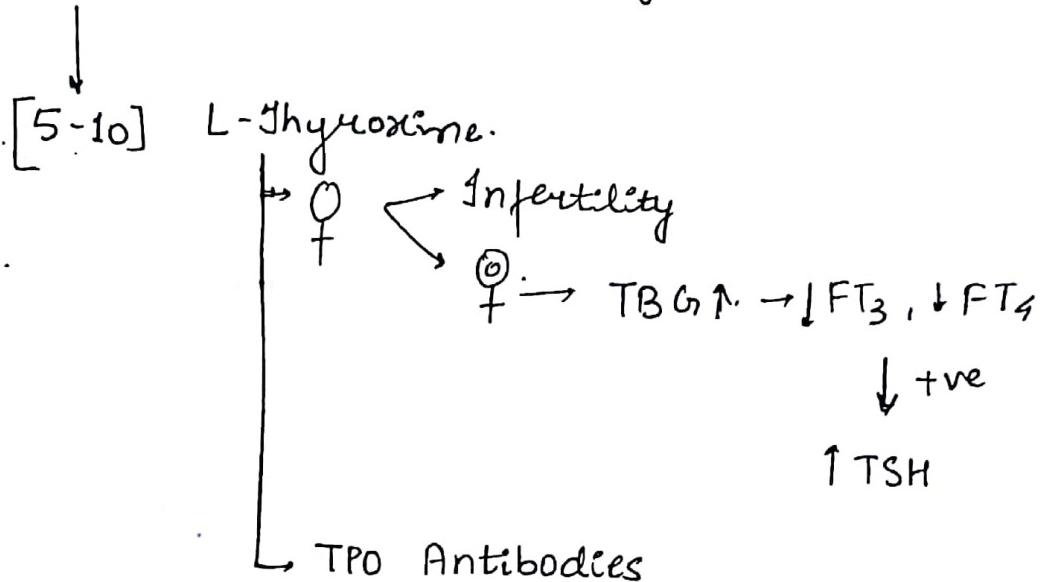
## SUBCLINICAL HYPOTHYROID

404

↑ TSH, [FT<sub>3</sub>, FT<sub>4</sub>] low (N)

Rx-

TSH > 10 ⇒ Start L-thyrc



## ADRENALS

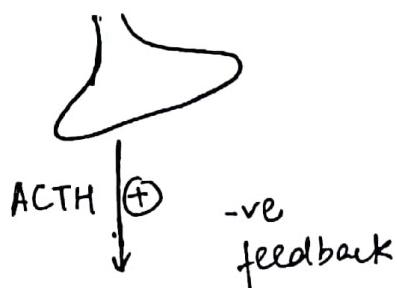
405

### CUSHING SYNDROME

LOSS of -ve feedback

#### ETIOLOGY

A> EXOGENEOUS / IATROGENIC [M/c/c]



B> ENDOGENEOUS

↓  
ACTH

↓  
DEPENDENT (90%)

↓  
INDEPENDENT (10%)

Pituitary Adenoma 75%  
F:M = 4:1  
M/c endogenous cause  
→ ECTOPIC ACTH 15%

↓  
ADRENAL F:M = 4:1  
Adenoma (5-9%)  
CA (1%)  
Hyperplasia (<1%)

M/c malignancy → small cell Ca  
of Lung

- medullary ca of thyroid

- Phaeochromocytoma

- CARCINOIDs
  - Bronchial
  - Ghymus
  - Pancreatic

M/c/c → CUSHING DISEASE

Cushing Syndrome due to Pituitary Adenoma.

C/F :-

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↑ CORTISOL → ↑ Gluconeogenesis

1) PROTEIN → MYOPATHY (proximal)

↳ s/c Tissue tear = **STRIA**E Purplish colour due to rupture of vessels.

↳ THIN SKIN

↳ EASY BRUISING.

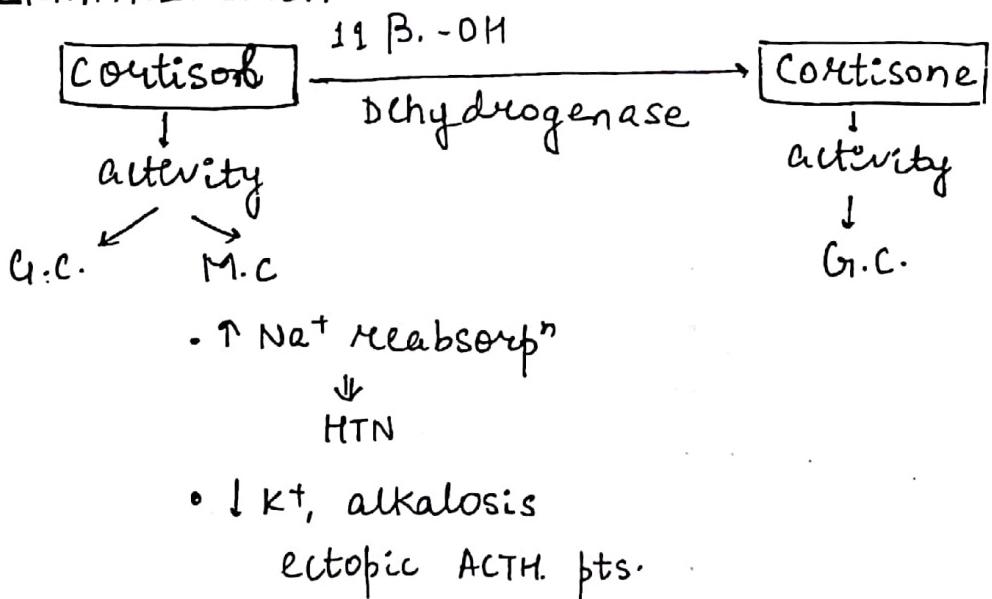
2) FAT Redistribution of fat

CENTRIPETAL OBESITY

↳ BUFFALO HUMP  
↳ MOON LIKE FACE

3) DM

4) HYPERNATREMIA



5) ♀

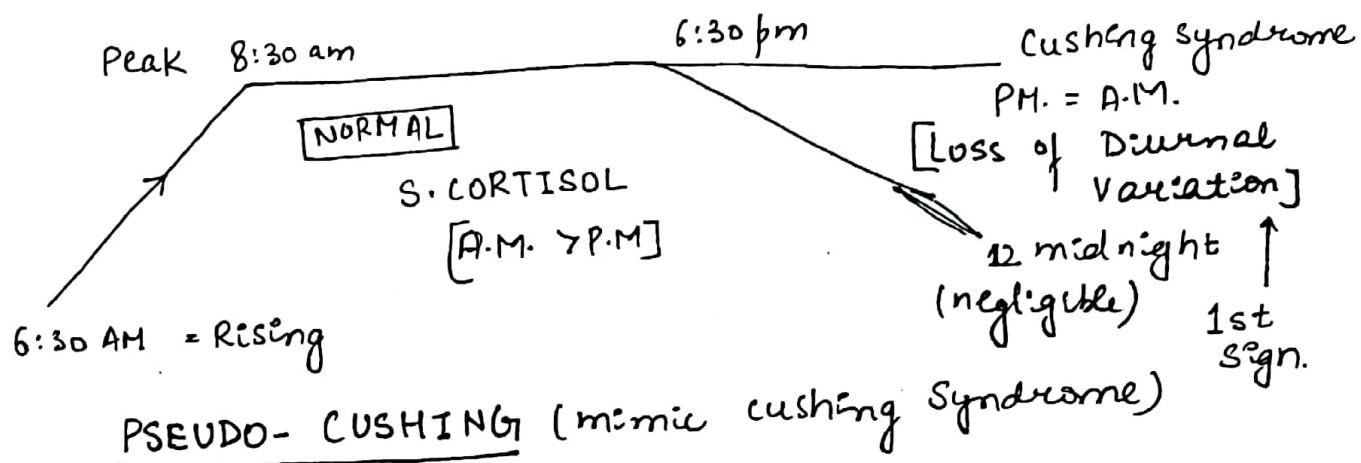
Oligomenorrhea —————> Amenorrhea  
Hirsutism

6) CNS -

↑ appetite  
↓ sleep

Euphoria  
[Psychosis]

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Chronic ~~alcoholics~~ alcoholics

Cirrhotic pts.

Pts  $\in$  Hyperthyroidism

Pt  $\in$  Depression.

### CLINICAL SUSPICION OF C.S.

WEIGHT GAIN = Thin skin > HTN  
(80%) (80%) (75%)

1st M/c symptom

> central obesity  
(50%)

>  $\downarrow K^+$ , alkaloses  
(15%)



SCREENING TEST

**SP1 SCREENING TEST**

408

- 24 HR. URINARY CORTISOL ↑↑
- MIDNIGHT S. CORTISOL ↑
- ORAL DEXA CHALLENGE TEST [BEST]

1mg DEXAMETHASONE @ 11:00 PM

(oral) ↓

S. CORTISOL @ 9:00 AM

$$\lceil \textcircled{N} = \textcircled{N}$$

$$\lceil \text{C.S.} = \uparrow \quad (\text{due to loss of -ve feedback})$$

↓

**CONFIRMATORY**

4mg 0.5mg DEXA I/V hourly × 2 days

↓

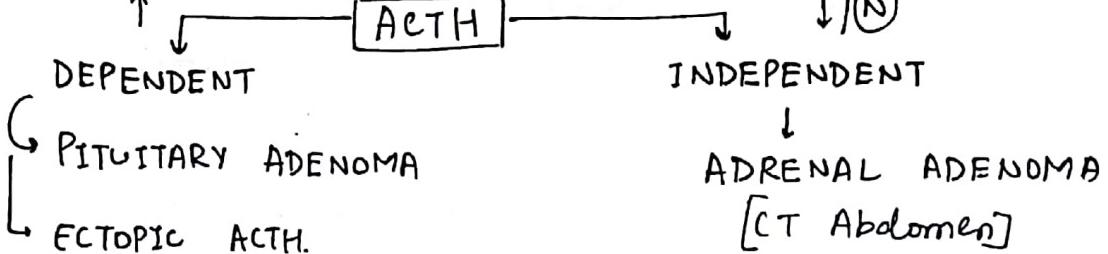
S. cortisol →  $\textcircled{N} = \text{C.S.} \ominus \ominus$

↓  $\uparrow = \text{C.S.} \oplus \oplus$

**[LOW DOSE DEXA TEST]**

↓  
**ETIOLOGY** H/o - exogenous

**ACTH**



MRI can't visualize pituitary adenoma (2-5mm)

**1) INF- PETROSAL SINUS SAMPLING (IPSS)**

**(CRH)**

↓ (+)

ACTH

↓ Sample → Petrosal sinus (PS)

→ Peripheral vein (PV)

RATIO

409

$\frac{PS}{PV}$  ↑ ↓ ⇒ Increased  
PITUITARY ADENOMA

$\frac{PS}{PV}$  ↓ ↑ = Decreased.  
ECTOPIC ACTH

2mg DEXA I.V. 6hrly × 2 Days

↓  
S. ~~cortisol~~ cortisol ↓ = Pituitary Adenoma  
unchanged = Ectopic ACTH.

2) High Dose DEXA TEST

## PITUITARY ADENOMA

## ECTOPIC ACTH

C/F

ONSET → Insidious

Acute

PROGRESSION → Slow

Rapid

HYPERPIGMENTATION → +

+ + + +

IPSS

 $\frac{PS}{PV}$  ↑
 
 $\frac{PS}{PV}$  ↓
 

HIGH DOSE DEXA +ve  
TEST Response

Unchanged.

Rx

Ketoconazole  
Metapyrone  
Etomidate  
Mirtazapine

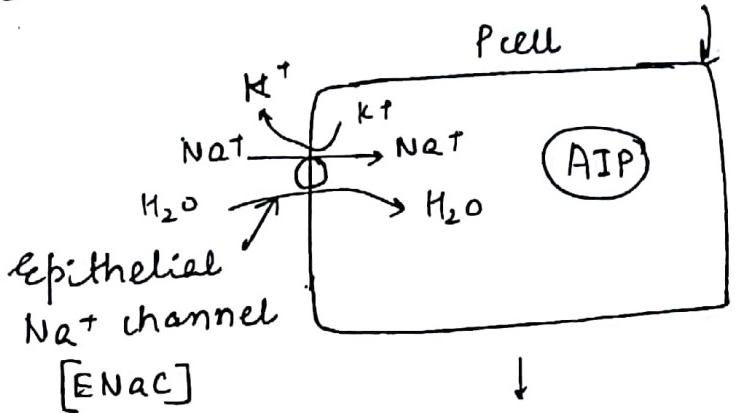
⊖ cortisol  
synthesis

# HYPERTENSION

410

2°

↓ volume → ↑ Renin → ↑ Aldosterone



AIP = aldosterone induced protein.

Epithelial  
 $\text{Na}^+$  channel

[ENAC]

$\downarrow$   
 $\uparrow \text{Na}^+ \rightarrow \uparrow \text{H}_2\text{O}$

$\downarrow$   
volume (N)

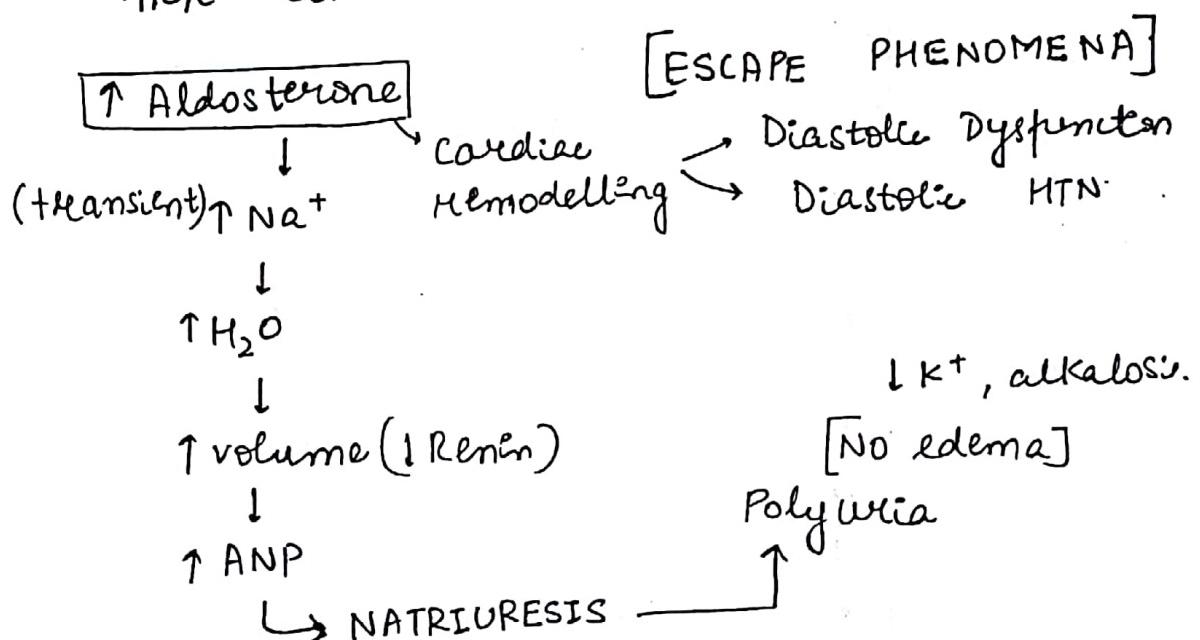
1°

← Mi.c.c.

→ BIL Adiopathic cortical Hyperplasia (60%)

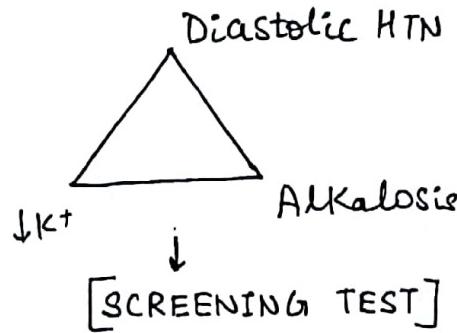
2) Adrenal Adenoma (40%)

M/c/c - CONN SYNDROME



## CLINICAL SUSPICION

411



ALDOSTERONE RENIN RATIO (ARR) > 20

↓  
[CONFIRMATORY TEST]

2 Litres of Normal Saline x 4 Hours

↓  
↑Volume → ↓ Renin - ↓ Ald. ⇒ N

↓

NO suppression of Aldosterone

↙ [SALINE INFUSION TEST]

↓  
ETIOLOGY

↓  
CT Abdomen

ADE NOEMA



<40 yrs

UL

ADRENELECTOMY

>40 yrs [Incidentaloma]

Adrenal venous sampling

ALDOSTERONE

HIGH

HYPERPLASIA.

Rx - Aldosterone (-)  
↳ Spironolactone  
↳ Triamterene

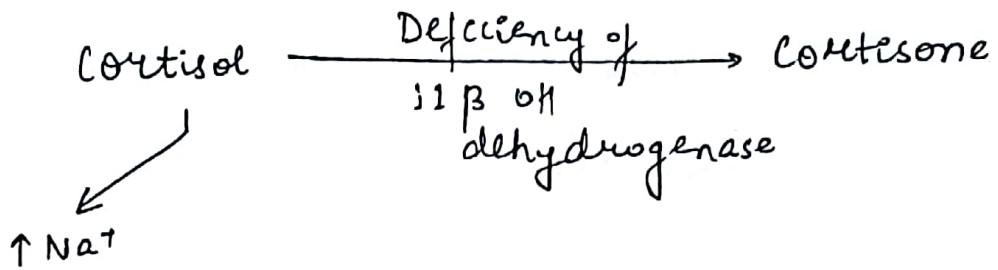
N = watch

Medical Therapy

DfD

412

1) Syndrome of apparent Mineralocorticoid excess  
[SAME]

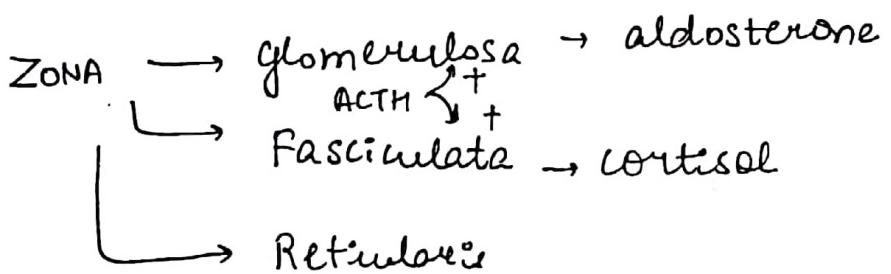


Lk<sup>t</sup>, Alkalosis

R = STEROIDS → ↓ ACTH

!  
I corteggi.

27 Glucocorticoid Remediable Aldosteronism [GRA]



Rx - STEROIDS → ↓ ACTH → ↓ Aldosterone

## 37 LIDDLES SYNDROME

↑ Functioning of ENAC → ↑  $\text{Na}^+$   
↓  $\text{K}^+$ , alkalosis.

# ADRENAL INSUFFICIENCY

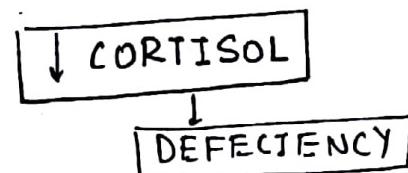
413

*ADDISON DISEASE*  
ADRENAL

Autoimmune (Mcc In world)  
TB (Mcc In India)

**2°**

PITUITARY  
 - Surgery  
 - Trauma  
 - Radiation  
 - Apoplexy



**↓ G.I.C.** ← Activity → **M.C. ↓**

↓ GLUCOSE

↑ Protein Breakdown

↓ Cal. loss

Thin

**ASTHENIA**

M/C + 1st  
symptom

lethargy  
Fatigue

↓  $\text{Na}^+$  ← salt sweating  
 ↑  $\text{M}/\text{C}$  Biochemical  
 Ab(N)

↓ ECF

↓ BP

[ $\text{T K}^+$ , acidosis]

**↑ ACTH**

Hyperpigmentation. (localised)

↳ Oral mucosa

Conjunctiva

Palmar crease

Nipple areola Region

moles, scars

ACTH administration

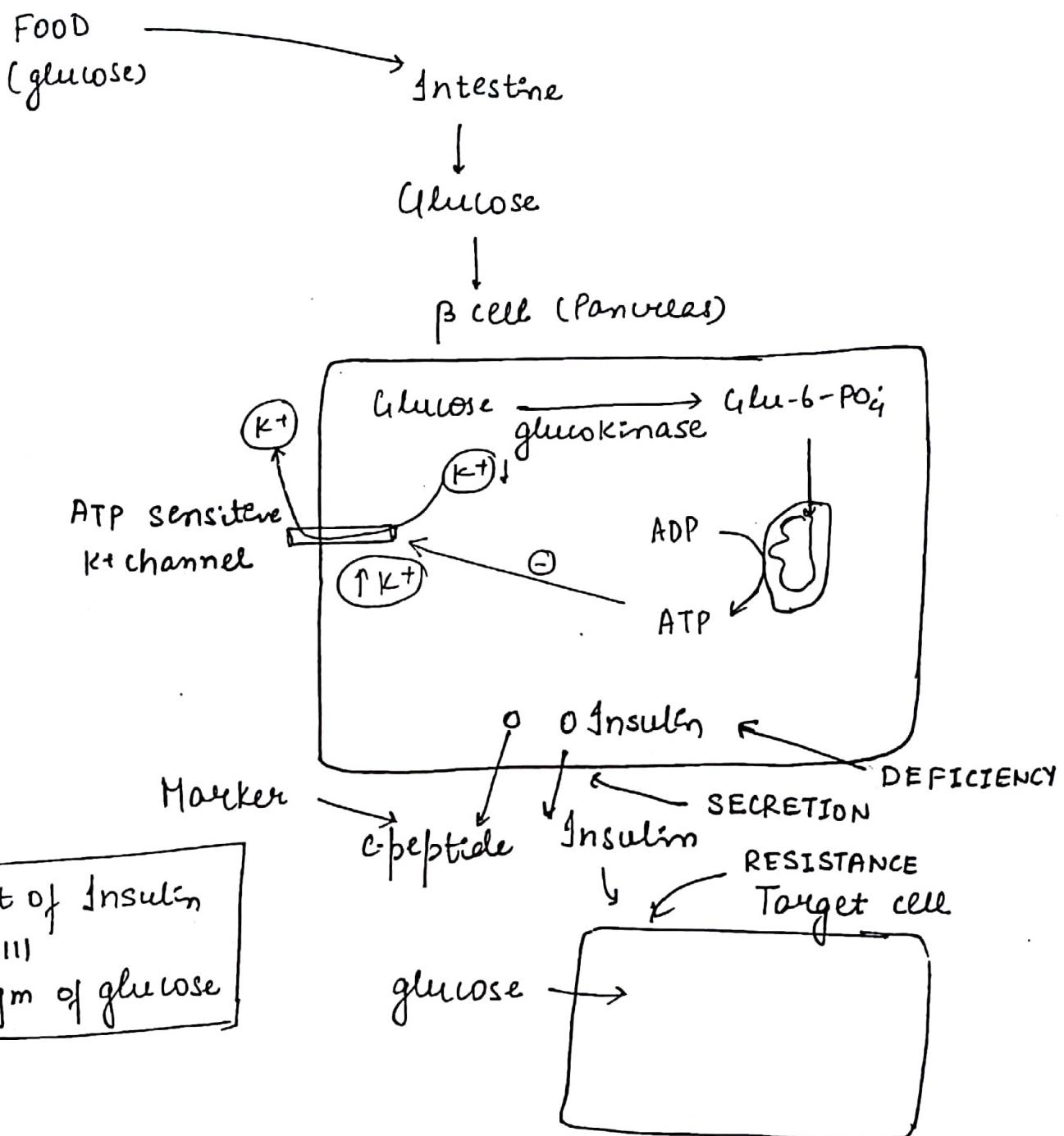
$\hookrightarrow$  (N)  $\rightarrow$  CORTISOL  $\uparrow$   
 $\hookrightarrow$  Addison's pt  $\rightarrow$  CORTISOL (unchanged)

[ACTH STIMULATION TEST] COSYNTROPIN / SYNACTHEN  
~~Diagnostic Test~~ TEST

$R_x$  = STEROIDS

Hydrocortisone (DOC)

# DIABETES MELLITUS (DM)



Deficiency = TYPE-I

Insulin ↑ → II

Secretion → TYPE-II  
Resistance

| <u>TYPE - I</u>                      |         | <u>TYPE - II</u>              |
|--------------------------------------|---------|-------------------------------|
| - $\beta$ cell Destruction<br>(>90%) |         | secretory Defect              |
| - HLA Mediated                       |         | Insulin Resistance            |
| Anihbulinemia                        |         | Hypersenslvenemia             |
| Age of Onset                         | <30 yrs | >30 yrs                       |
| Habitus                              | thin    | obese                         |
| Family His.                          | ⊕       | ⊕ ⊕ ⊕ ⊕                       |
| HTN                                  | ⊖       | ⊕                             |
| Dyslipidemia                         | ⊖       | ⊕ [↑ TG → ↓ HDL]              |
| DKA                                  |         | Hyperosmolar Non-Ketotic Coma |

|                              |                   |                                             |                  |
|------------------------------|-------------------|---------------------------------------------|------------------|
| 20 yrs                       | → 25 yrs          | 30 yrs                                      | → 35 yrs         |
| RBS ↑↑↑                      | RBS - controlled. | RBS ↑↑↑                                     | RBS ↑↑↑          |
| K.B. ⊕                       | Insulin ↓↓        | K.B. ⊖                                      | OHA ↑↑↑          |
| Obese                        | (OHA)             | OHA                                         | Insulin (Type 1) |
| Insulin (Type 1)             | (Type 2)          | (Type 2)                                    |                  |
| KETOSIS PRONE DIABETES (KPD) | 1.5 DM            | LATENT AUTOIMMUNE DIABETES IN ADULTS (LADA) |                  |

## MATURITY ONSET DIABETES IN ADULTS (MODY)

Onset 5-15 yrs of Age.

Thin

OHA Response

AD Inheritance

DKA (-)

HTN (-)

6 types of MODY

↓

TYPE 3 (M1c type)

↓

HNF -1 $\alpha$  Deficiency

## TYPE-3 DIABETES / BRAIN DIABETES / ALZHEIMER

Insulin Resistance, Deficiency

↓

PPT the cond?

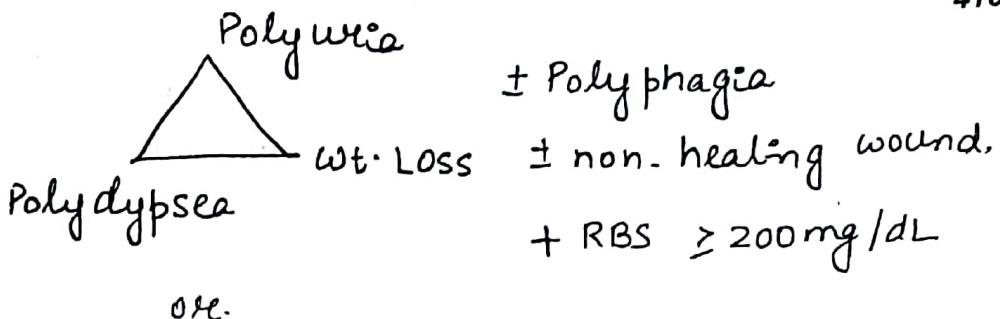
## TYPE-4

Elderly >60 yrs.

OHA response (minimum dose)

## DIAGNOSIS

418



Fasting 8 hrs  $\leftarrow$  Fasting BS  $\geq 126 \text{ mg/dL}$   
or

[Oral GTT]

75gm glucose (oral)  
 $\downarrow$   
2 hr BS  $\geq 200 \text{ mg/dL}$ .

or

[HbA<sub>1c</sub>]  $> 6.5\%$   
[glucose + globin]

## ACUTE COMPLICATION OF DIABETES

[DIABETIC KETOACIDOSIS]

Type-1

① RBS = 250 - 600 mg/dL (Reliable)

② Ketone Bodies  $\rightarrow$  Blood  $\rightarrow$  KETONEMIA  
 $\rightarrow$  Urine  $\rightarrow$  KETONURIA

③  $\downarrow$  pH (Best bedside)

C/F

1) nausea, vomiting (persistent)

K.B.  $\oplus$  CTZ

2) Abdominal Pain  $\pm$  Tenderness

3) ↑ HR

4) TRR [KUSMALL BREATHING]  
Metabolic acidosis → Resp. alkalosis  
 $\text{CO}_2 \rightarrow \begin{cases} \textcircled{1} \text{ acidosis} \\ \textcircled{1} \text{ alkalosis} \end{cases}$

5) Fruity odour → due to acetone

6) **Dehydration** (severe)  
H/c C of mortality

**Rx** -

1) I.V. fluids (4-6 L)  
 $\downarrow$  0.9% NS → To prevent ↑  $\text{Na}^+$ , ↑  $\text{Ca}^{2+}$  → 0.45% NS  
 Most effective Rx. 4-6 hrs → To prevent hypoglycemia  
 $\times \text{ RL} \times$        $\boxed{5\% \text{ Dextrose}}$   
 $\times$                   RBS < 200

2) Insulin

Regular → 10 units/IV Bolus  
 $\downarrow$   
 0.1 U/kg/hr

3) KCl @ 20-40 meq/hr.

4)  $\text{NaHCO}_3$   
 $\text{pH} < 7$

# HYPEROSMOLAR NON-KETOTIC COMA

TYPE=2

RBs = 600 - 1000 mg/dL

↑ Sr. Osm.

KB (-)

Altered sensorium

Rx =  
1) IV fluid (6-10L)

2) Insulin

## CHRONIC COMPLICATION

DIABETIC NEUROPATHY

### (A) POLYNEUROPATHY

Distal Symmetric sensory  
(M/C type)

1st S lost

glove  
stocking }  
S Loss

Vibration

[128 Hz Tuning Fork]

PARAESTHESIA

→ ANAESTHESIA

Rx

1) Improved Glycemic control

2) Pain L AED = Pregabalin

TCA = Amitriptyline

## (B) MONONEUROPATHY

M/c cranial N/V

 $\underline{\text{III}} > \underline{\text{VII}}$ 

[Pupillary sparing]

Mononeuritis multiplex = Patchy involvement of

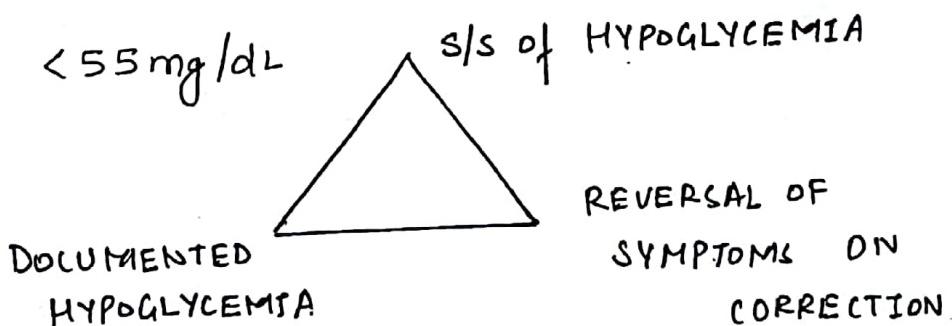
↳ M/c/c - metabolic = DM [(B) in India + world]

Infective = LEPROSY

vasculitis = POLYARTERITIS NODOSA

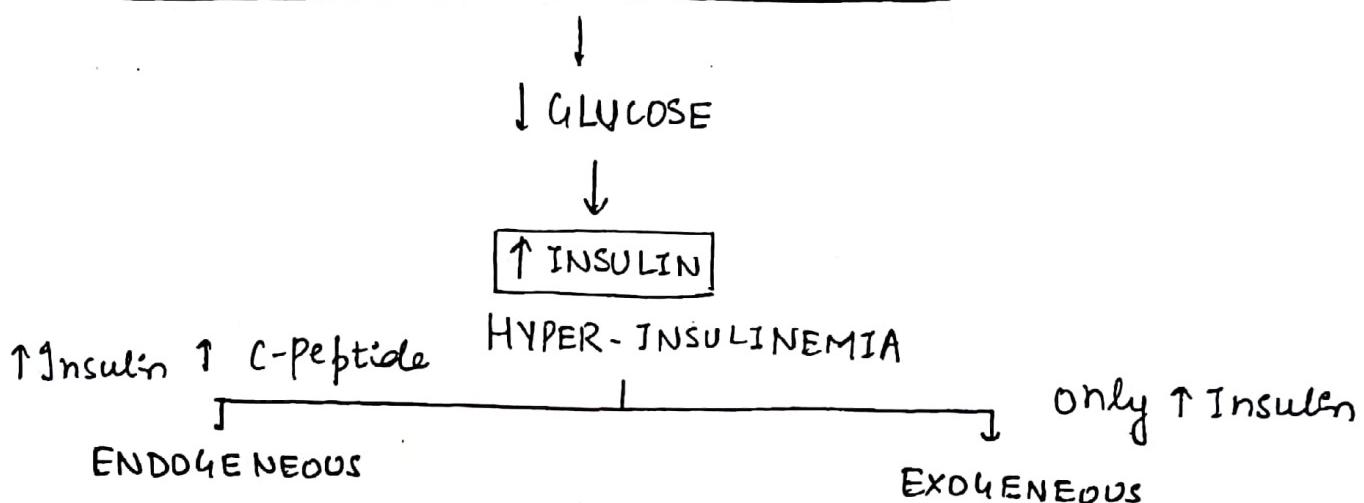
## (C) AUTOIMMUNE AUTONOMIC NEUROPATHY

Hypoglycemic unawareness

 $\beta$ -G avoided in diabetic pts.Intensive control is avoided  $\Rightarrow$   $\uparrow$  Risk of hypoglycemiaHYPOGLYCEMIAWHIPPLES TRIAD

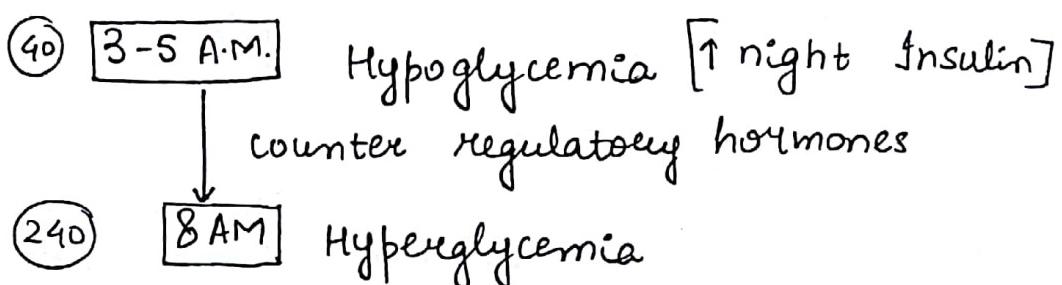
- 1) ↓ Insulin
- 2) ↑ Glucagon
- 3) ↑ Cortisol  
Epinephrine  
GH

**EXTENSIVE FASTING  $\times 72$  hours**



Insulinoma  $\rightarrow$  Radiological  
Sulphonylurea Induced  
↳ SU Levels

### SOMOGYI EFFECT



Rx = Long Acting Insulin.

## DAWN PHENOMENA

(240)

3-5 AM Hyperglycemia

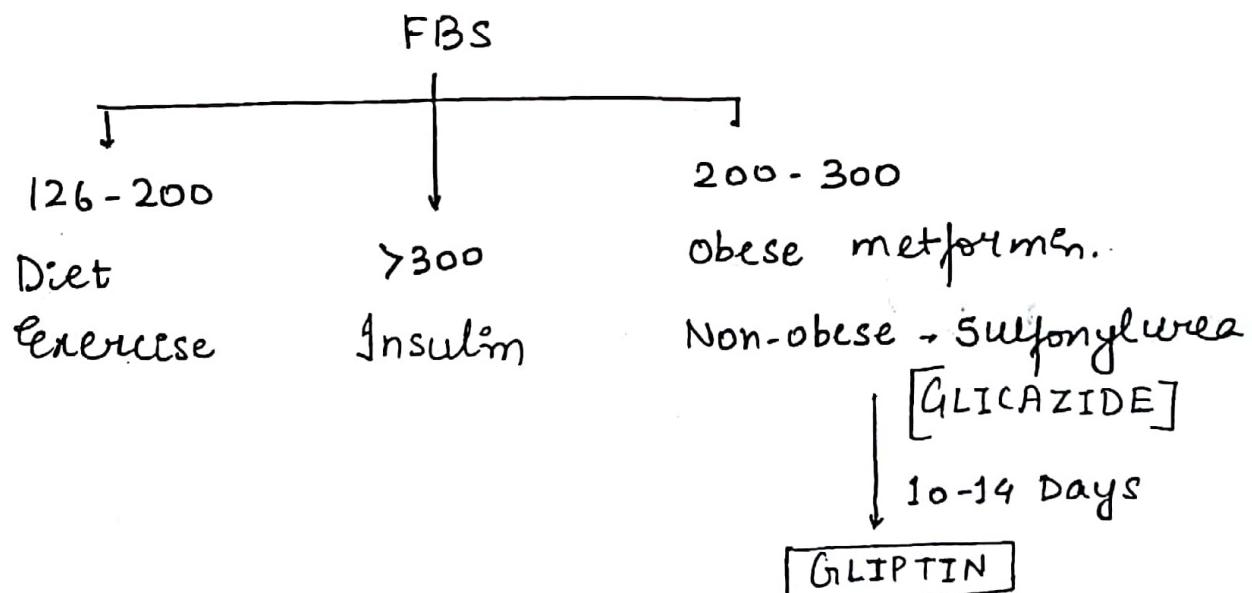
↓  
 Insulinopenia  
 ↓  
 Insulin resistance

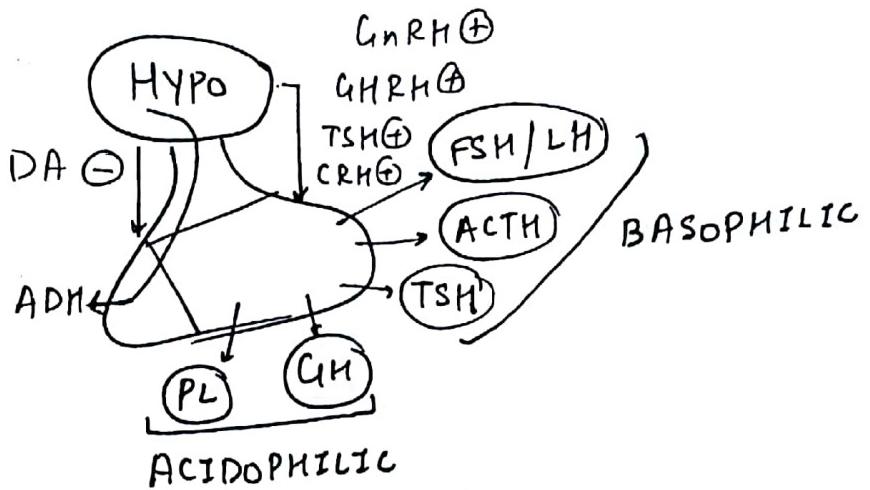
(340)

8 AM Hyperglycemia

Rx = ↑ night insulin + insulin sensitizer

## Rx of TYPE-2





### STALK LESIONS

↑ Prolactin

Hypothyroidism (central)

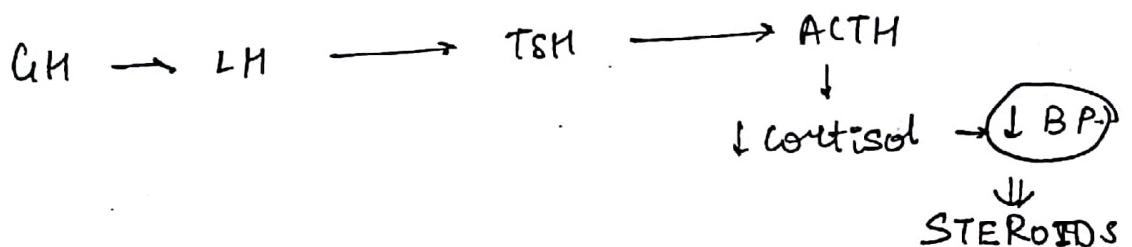
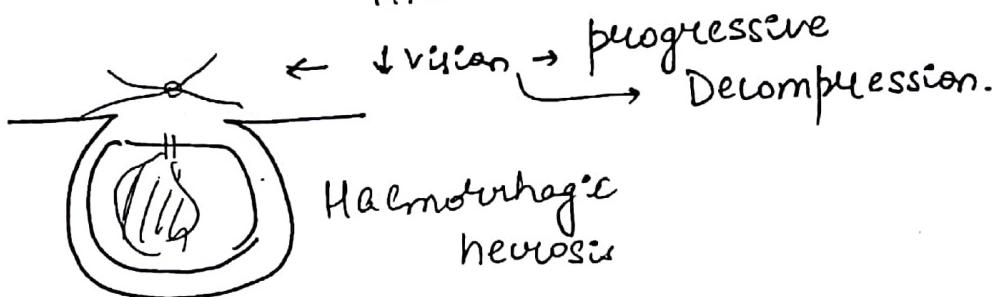
↓ glucose

↓ BP

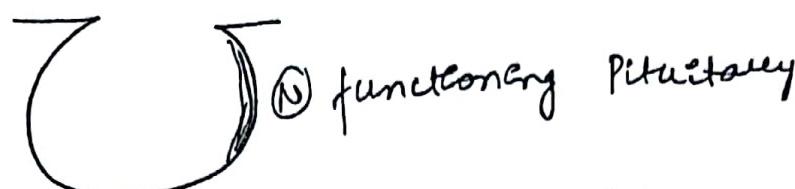
Central DI

PITUITARY APOPLEXY  
↳ SHEEHAN SYNDROME

↑ Incidence = Sickle cell Disease ]  
DM ]  
HTN ]  
Predisposing Factors



↓  
after few months



⑩ functioning Pituitary  
EMPTY SELLA SYNDROME (Incidental finding)



# MEDICINE (GIT)

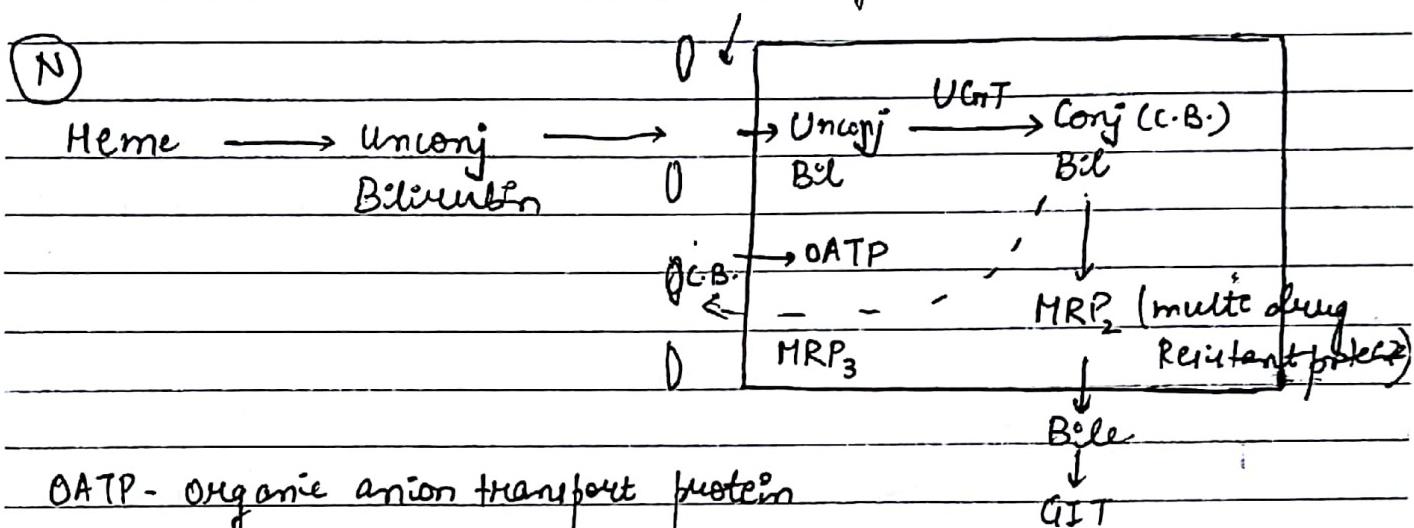
427

## Liver

## Intestine

- \* Disorder of Bilirubin met
- \* Acute Viral Hepatitis
- \* Chr. hep / cirrhosis
- \* Comp' of Liver failure
- \* Malabsorption syndrome
- \* Diarrhoea
- \* GI "infe"
- \* IBD
- \* IBS

## BILIRUBIN METABOLISM space of Disse



OATP - organic anion transport protein

## DISORDERS OF BILIRUBIN METABOLISM

### I ↑ Unconjugated Bilirubin

> Increased synthesis -

a) Hemolytic anaemia → ↑ premature destruction of RBCs in periphery

b) Ineffective erythropoiesis → ↑ premature destruction of RBCs in Bone marrow

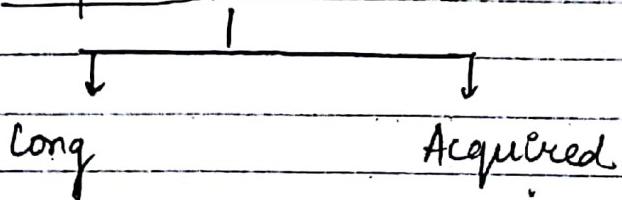
Cause

- ⇒
  - Thalassemia
  - Megaloblastic anaemia
  - Severe Fe def.
  - Pb poisoning

c) Large haematoma

d) Lobar pneumonia (TRBC destruction in exudate)

ii) ↓ Uptake :-



Gilbert Syndrome -

Duage- Rifampicin

Probenecid (prophylaxis for gout)

Ribavirin (for HPS C virus)

3) ↓ UGT :- (UDP Glucuronyl Transferase)

\* Cong. causes -

Crigler Najjar I

CN II G<sub>6</sub>P

Gilbert Syndrome

UGT

0%

50%

33%

activity

Mode of inheritance

AR

AR

Both (AR>AD)

S.Bil (Total)

>20

6-20

<4

Kernicterus

(+)

Rare

(-)

Mortality

Before 1 year

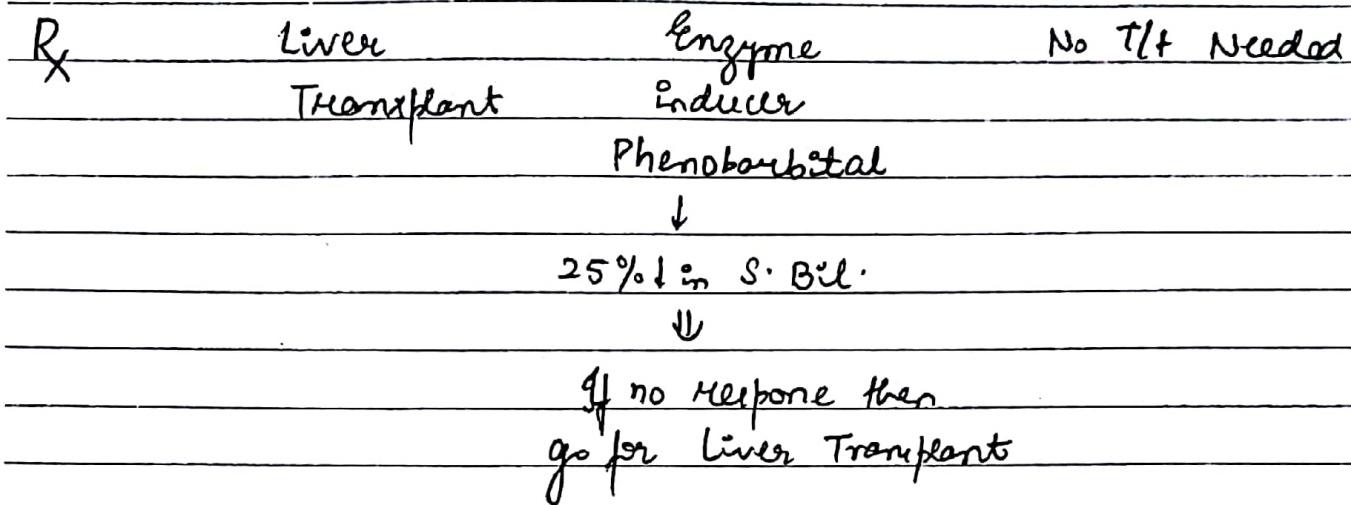
or about 1/4 -

Adulthood

Not ↑.

Important

| CN I     | CN II | Gilbert Syndrome      |
|----------|-------|-----------------------|
| Inv.     | N     | Lipofuscin<br>pigment |
| Liver B. |       | = Brown colour        |



### \* Acquired causes :-

1) Drugs - Gentamycin  
 Chloramphenicol  
 Pregnanedione

2) Breast Milk Jaundice (Self-Limiting)

FA (-) → UGT of neonate →

No need to stop feeding

3) Lucey Driscoll Syndrome :- (Self Limiting)  
 Maternal Serum Ab (-) UGT of neonate

II) ↑ Conjugated Bilirubin (Isolated).

Liver enzymes (N)

1

Dubin Johnson  
Syndrome

Rotor Syndrome

Mech - Mutation of MRP<sub>2</sub>.

② Mutation of OATP

Mode of inheritance AR

AR.

S-Bil. <4

<4

Kernicterus (-)

(-)

Mortality not ↑

not ↑

Inv

Liver Bx Black Pigmentation.

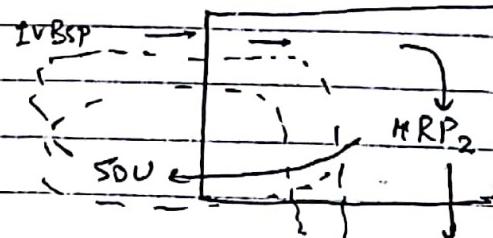
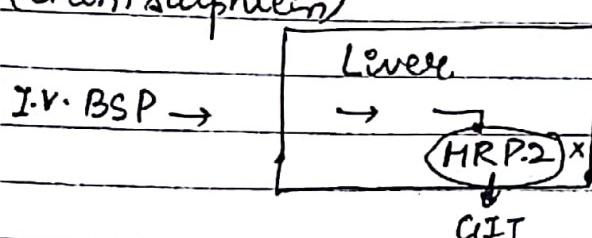
Normal.

(Epinephrine metabolite N)

excreted by MRP<sub>2</sub>)

BSP clearance  
test

(Bromsulfophen)



(N) BSP clearance ≤ 90 min

∴ MRP<sub>2</sub> absent, hence no clearance of BSP

Delayed clearance of BSP

Rx not Req.Not Req.

Q. E feature will suggest cause of ↑ of unconjugated BIL except :-

a) GB pigmented stones (H. anaemias) True

b) P/s → spherocytes (H. anaemie) True

~~c) Acute hep c viral infection Enzyme ↑ + conjug. ↑~~

d) H/o goit - True (Probeneid)

### ACUTE VIRAL HEPATITIS

caused by hep A to E

Hep A

① Mode of - H/c Feco-oral  
Transmission.

Hep E

H/c Feco-oral

sewer line

② Transmission to - common  
close contact

Rare ↓  
community  
spread.

③

'New epidemic in  
community'

④ Rare - • Blood Transfusion  
Viremia during late  
incubation period

Vertical

• Sexual

⑤ Not a mode  
of transmission

Vertical

BT  
Sexual

|                                                                       | Hep A                                    | Hep E                                                                                   |
|-----------------------------------------------------------------------|------------------------------------------|-----------------------------------------------------------------------------------------|
| C/F                                                                   | M/c cause of Ac. Viral Hep. in children. | M/c of Ac. Viral Hep. in adults.                                                        |
|                                                                       | [M/c of Viral Hep - B]                   | M/c of Ac. Viral Hep. in<br>♂                                                           |
|                                                                       |                                          | [M/c of Viral Hep in ♂ = B]                                                             |
| Relapsing Hepatitis                                                   |                                          | Cholestatic hepatitis.<br>Swollen hepatocytes cause obstruction to intrahep. Bile flow. |
| 2 clinical episodes by same virus in ac. phase (<6mth)                |                                          | [ALP also ↑].                                                                           |
| Inv                                                                   |                                          |                                                                                         |
| Serology                                                              | IgM Anti-HAV<br>= Acute Hep. A infect    | IgM Anti-HEV<br>= Acute Hep E infect                                                    |
| IgG Anti-HAV - Pt is immune                                           |                                          | IgG Anti-HEV - Pt is immune                                                             |
| ↓ Possibilities                                                       |                                          |                                                                                         |
| • Post vaccination ✓                                                  |                                          | • ↑ ✓                                                                                   |
| • Remote recovered past infect ✓                                      |                                          |                                                                                         |
| • Chronic infection. X (virus + > 6mth)                               |                                          | X                                                                                       |
| Complications.                                                        |                                          |                                                                                         |
| 1) Fulminant hepatitis - 0.1%<br>(encephalopathy < 2 wks of Jaundice) |                                          | ♂/non ♀ → 1-2%<br>♀ → 10-20%                                                            |

|                                                  |    |    |
|--------------------------------------------------|----|----|
| 2) Chronic Hep                                   | 0% | 0% |
| (Viral is +ve for >6 months<br>+ Liver damage +) |    |    |
| 3) Carrier.                                      | 0% | 0% |
| (Virus + > 6 months<br>Liver damage -)           |    |    |

~~LMP Topic~~

### Hep B

Mode of ① M/c - vertical  
Transmission

Mother HbeAg +

Risk - 90%

AntiHbe Ab

Risk - 10%

① M/c - Percutaneous.

Needle

1.8 - 6%  
Milk

Viable < 4 days.

>  
BT

1 in 18 lac of  
Blood units.

transfused.

② Percutaneous

Needle

6 - 30% Milk

Viability of virus  
7 days.

M/c BT related risk = (B)

HIV

Needle IV drug  
accidental

RISK.

0.6%

0.3%

1 in 22 lac

|                                                                             | MOT | HIV    | Risk               |
|-----------------------------------------------------------------------------|-----|--------|--------------------|
| (Some donors have low level HBsAg & it NOT detected by routine lab method). |     |        | vertical - 5% risk |
| ③ Sexual Variable                                                           |     | Sexual | 5% risk            |
| <u>Race. MOT</u>                                                            |     |        |                    |
| secreted into saliva = yes                                                  |     | yes.   |                    |
| Human Bite                                                                  | yes | yes.   |                    |
| <u>Not MOT</u>                                                              |     |        |                    |
| • Virus secreted into <del>stool</del> yes                                  |     | yes.   |                    |
| stools                                                                      |     |        |                    |
| • Feco - oral transmission                                                  | No  | No.    |                    |
| (destroyed in stomach)                                                      |     |        |                    |
| • Breast milk secreted yes                                                  |     | yes    |                    |
| " " transmission                                                            | No  | No     |                    |

Secreted:

- Q. All are transmitted by blood except
- a) Hep A      b) Hep A      c) Hep A  
 b) B      b) B      b) B  
 c) C      c) C      c) C  
 d) E      d) HIV      d) G

Q. All causes AVH, transmitted by blood except

- Hep A
- B
- C
- G. → never causes AVH.

Q. M/c mode of transmission of hep B

1) Vertical vs Horizontal

2) Vertical vs Percutaneous vs Sexual vs Human Bite

Q. Hep B not transmitted by

- Saliva
- Semen
- ~~Few-oral~~
- Breast feeding.

C/F

Hep B

Mcc of viral cause of HCC

express HBxAg

Hep C

Mcc viral cause of cirrhosis

[Mcc of cirrhosis = Alcohol]

Q p 53

④ Viral Replication

Mcc viral cause of Chro. Hep =  
(Prevalence wise)

Mcc AVH leading to Chro. Hep.  
or

Max. Risk of chronicity

Mcc of Carrier

Serum sickness like illness

↓ HBsAg + Ab

Joint pain + rash

Insulin Resistance by

- Insulin action

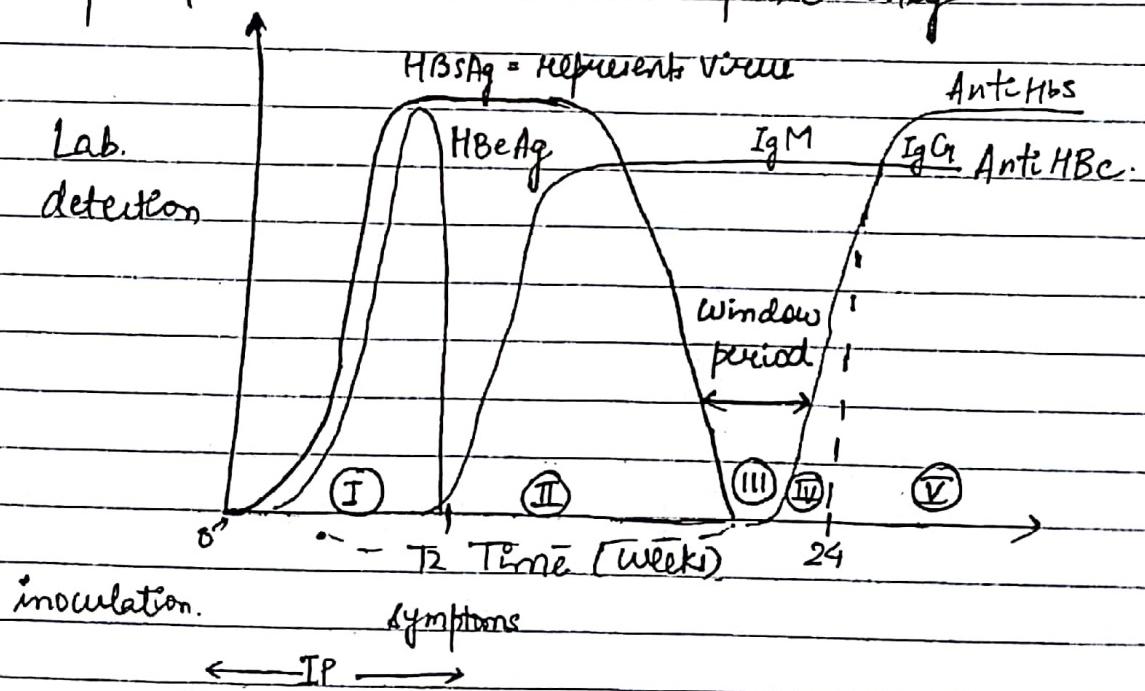
↑ Risk of T<sub>2</sub> DM

In children = LN + Hepatosplenomegaly  
+ Rash

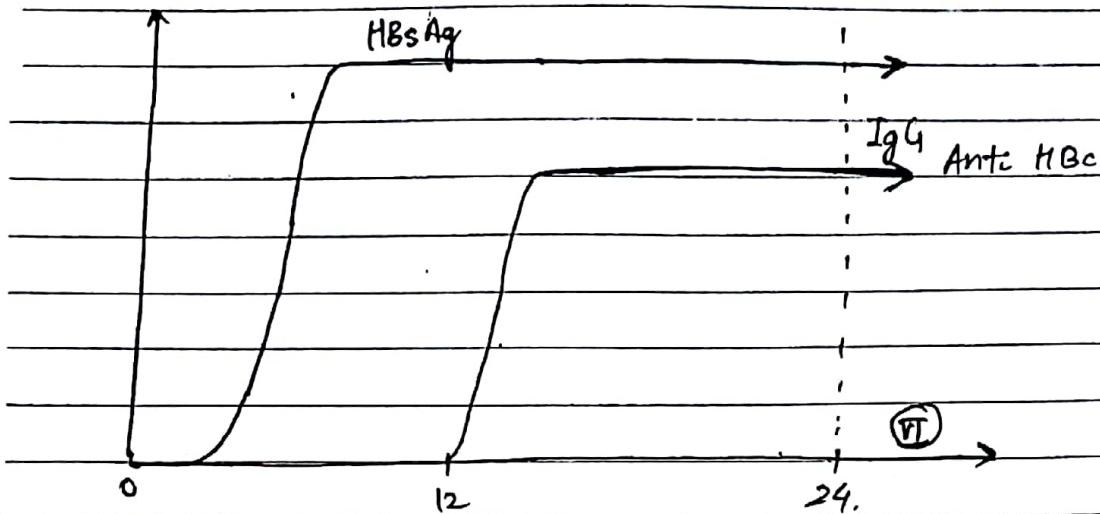
Gianotti Crosti Syndrome

### \* Serology of Hep B Infection

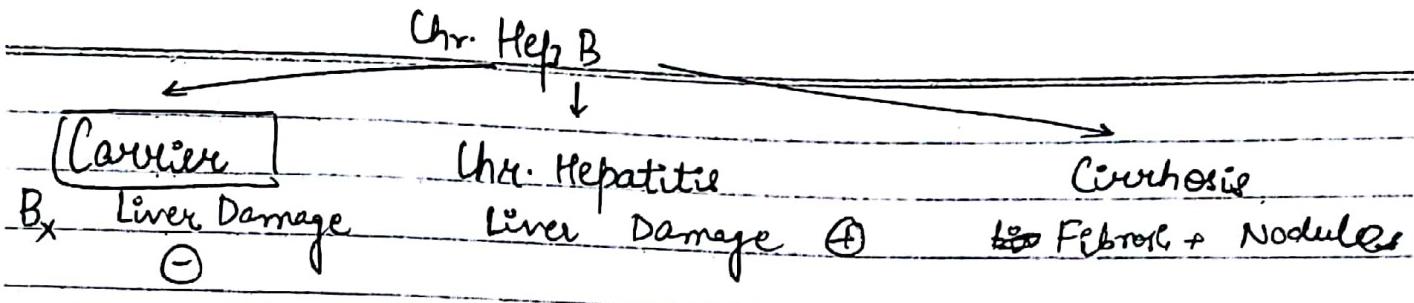
1) If Hep B limited to Acute phase only



2) If hep B converted to chronic infection



| <u>Phase</u>                      | <u>Marker</u>                                                       |
|-----------------------------------|---------------------------------------------------------------------|
| ① I.P.<br>Hep B infection         | HBsAg, HBeAg.<br>Earliest marker of HBsAg.                          |
| ② Acute (Symb)<br>Hep B infection | HBsAg, Ig M Anti HBc<br>Most reliable marker of Ac Hep B infection. |
| ③ Window period                   | Ig M Anti HBc                                                       |
| ④ Recovery period<br>of Ac. Hep B | Ig M Anti HBc, Anti HBs                                             |
| ⑤ Remote past infection           | Ig G, Anti HBc, Anti HBs ±<br>(disappear after year)                |
| ⑥ Chronic infection               | HBs Ag + Ig G Anti HBc                                              |



HAI (Histological Activity Index)  $\leq 3$

$\leq 3$

$> 3$

**Active**

**Inactive.**

Replication +

-

DNA copies.

$\geq 1000 / \text{mL}$

$< 1000 / \text{mL}$

Replication markers :-

- 1) Quantitative marker  $\rightarrow$  DNA copies. ← Most reliable replication marker
- 2) Qualitative marker  $\rightarrow$  HBe Ag.

exception Pre core Mutants of hep B virus

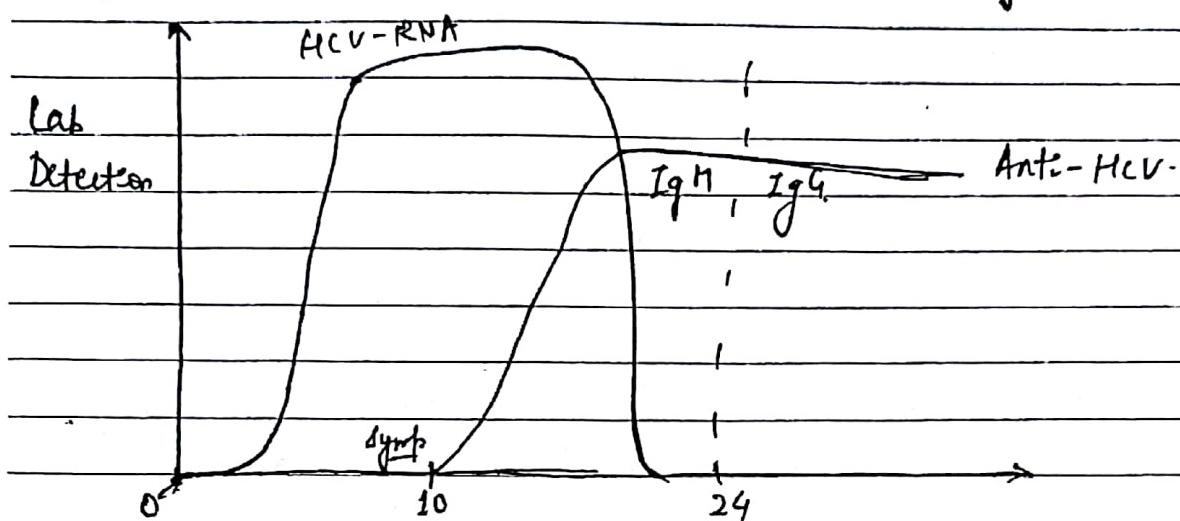


unable to make HBeAg but  
replication +

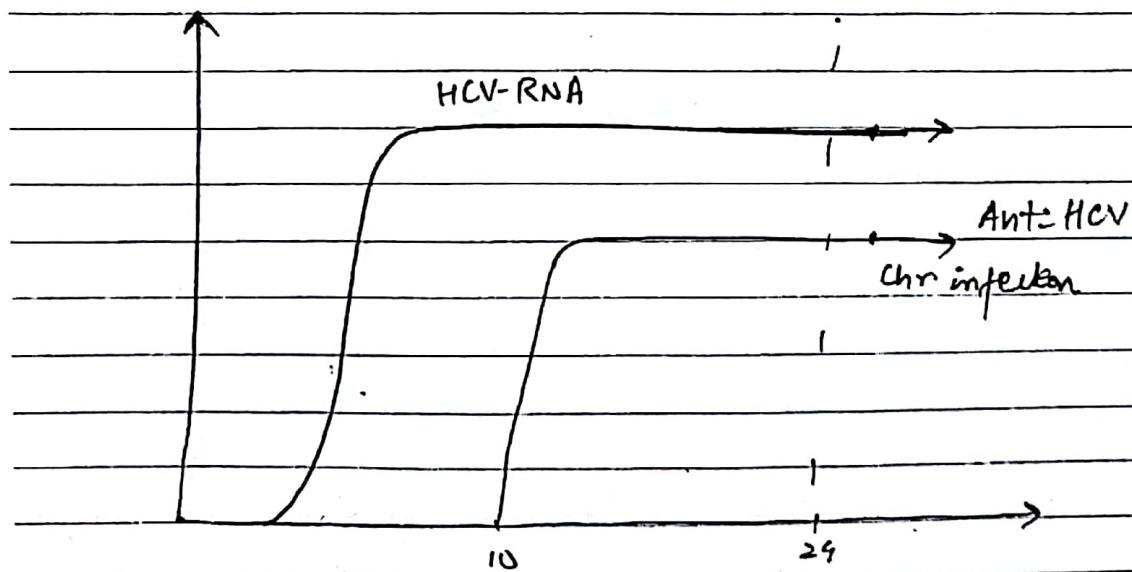
| DNA   | HBeAg | A                                   |
|-------|-------|-------------------------------------|
| ① (+) | (+)   | Relicative phase of (+) hep B virus |
| ② (+) | (-)   | Pre-core mutants of hep B           |
| ③ (-) | (-)   | Non-replicative phase               |

\* Serology of Hep c Infection :-

① If Hep c limited to Acute phase only



② If Hep c converted into chronic infection



| <u>Complications</u>  | <u>Hep B</u>            | <u>Hep C</u>              |
|-----------------------|-------------------------|---------------------------|
| ① Fulminant Hepatitis | 0.1 - 1%                | 0.1%                      |
| ② Chro. Hep           | 1 - 10%                 | 85% <sup>Inde</sup>       |
| ③ Carrier state       | 0.1 - 30%<br>Mean - 15% | 1.5 - 3.2%<br>Mean - 2.5% |

### Hep D

Inde

Mode of transmission - ① Percutaneous (Non-endemic zone) ✓  
 ② Close contact (endemic zone)

CF-

① H/c AVH leading to fulminant Hepatitis = D  
 or max risk

② Always associated to Hep B

Serology

① Co-infection - Acute hep D + Acute hep B  
 IgM Anti HDV                      IgM Anti HBC

② Superinfection - Acute hep D + Chronic hep B

IgM Anti HDV                      IgG Anti HBC

Comp

① Fulminant Hep. 5% in Co-infection.  
 20% in Superinfection

② Chr. Hep } → depend on Hep B-  
 ③ Carrier }

T/t

① AVH

→ Supportive Care (mostly self limiting).

I.v. fluid of choice = Dextrose as hypoglycemia risk  
 Min. Dextrose Req. = 150 g/day.

If 5% Dx = 3000 mL/d  
 (5g/100mL)

If 10% Dx = 1.5 L/day → Fluid of choice

If 25% Dx > 600 mL/day. → may cause thrombophlebitis.  
 ↳ not used for maintenance  
 reserved for emergency

2) Antivirals.

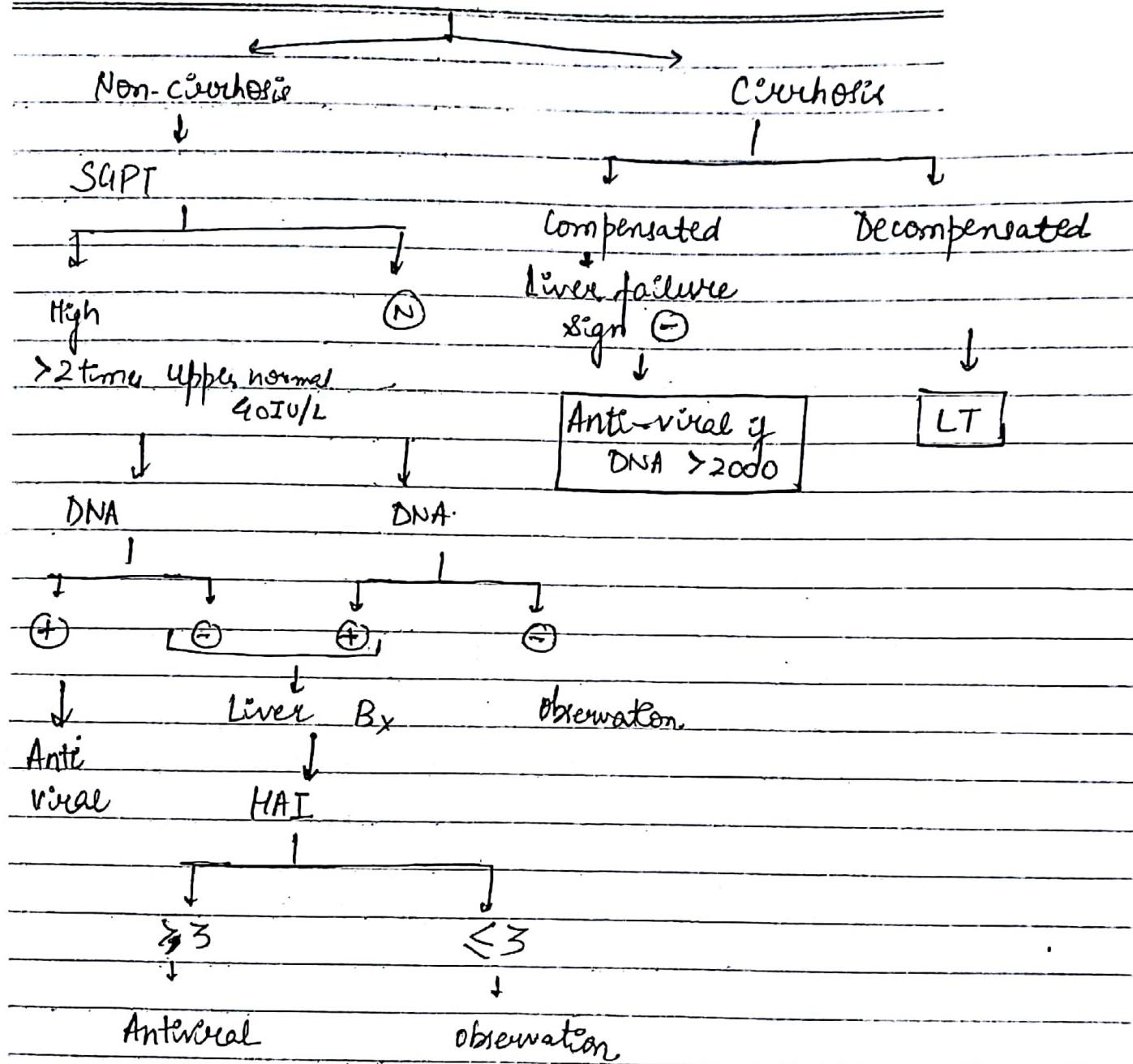
for Acute Hep C

Interferon α. 12-24 wks

LMR Topic

~~II~~ Chronic Viral Hepatitis

Approach to Chr. Hep B infection



DNA is (+) for Anti-viral if  $\geq 20,000 \text{ IU/mL}$  in HBeAg +  
 if  $\geq 2000 \text{ IU/mL}$  in HBeAg -  
 (Pre-core mutants).

### Anti-viral for Hep B

① Initiate = **(Monotherapy)** from 1st Line agents

1) Interferon α-

- oldest
- less effective in Cirrhosis

2) Entecavir -

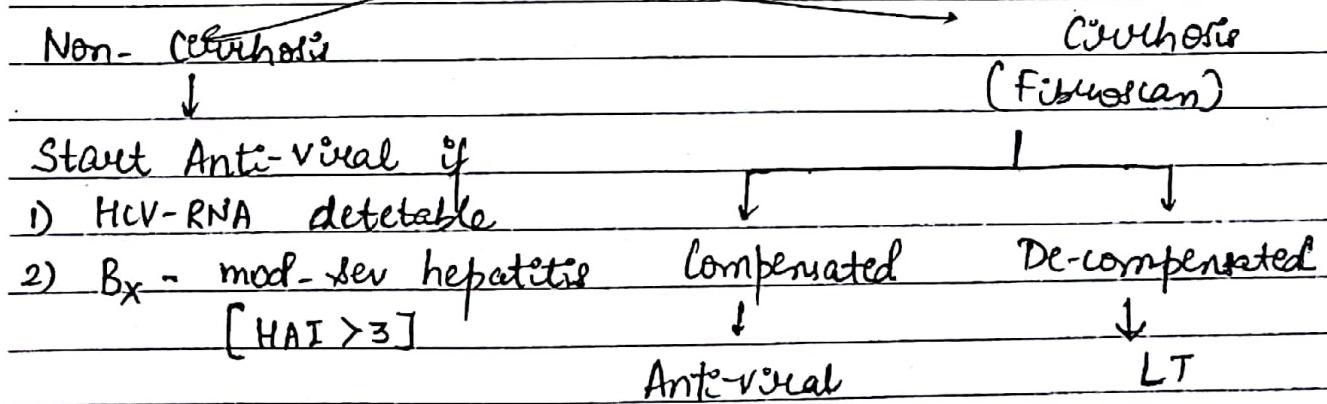
- most potent
- ↓ effectiveness in Lamivudine Resistant cases

3) Tenovovir → **DOC**

- safest + effective even in Lamivudine (R) cases

Duration  $\geq 1\text{yr}$

### **(II) Ch. Hep. C Infection**



### Antivirals for Hep C

Initiate = **(Dual)** therapy (oral combination therapy)

INFα → outdated nowadays

Sofosbuvir + Velpatasvir → effective in all 6 genotypes.

→  
Sofosbuvir + Daclatasvir

Duration - 12 wks. for all genotypes.

### FATTY LIVER



Alcoholic Liver

Disease

Patho

Dose → 40-80 g/d = fatty liver

80-160 g/d = cirrhosis

Duration 10-20 yrs

♀ → Dose is half.

Non-Alcoholic Liver Disease

Dose of → 0-20 g/d  
alcohol

Cause - Insulin Resistance

Stages

Mech

① Fatty Liver

Ethanol

① ⊖

TG deposit

② FA metabolism

↑ free FA → (TG)

② Hepatitis

F-L + enzymes ↑

Stages

Mech

① Fatty Liver

TG deposit ↑

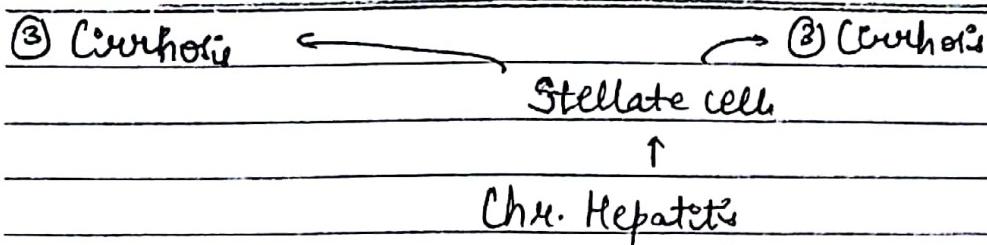
Insulin Resistance

↑ TG

Lipolysis

→ free FA ↑

② Hepatitis ← oxidative injury

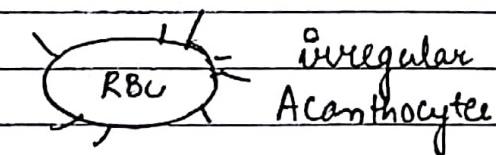
C/F

- 1) Peripheral Neuropathy  
 direct alcohol effect → pure sensory  
 Pyridoxine def.-induced by alcohol.

- 1) Causes of Insulin Resistance  
 (1) Metabolic obesity  
 (2) Type 2 DM  
 (3) Steroid ( $\ominus$  insulin action)  
 (4) **Hep C**

2. Zieve's Syndrome.

Deep Jaundice due to additional effect of haemolytic induced by alcohol



Q. C/C suggest alcohol as a cause of cirrhosis

(a) Spider angioma] due  $\uparrow$  estrogen  $\rightarrow$  ↓ catabolism in Liver  
 (b) Gynaecomastia

(c) Loss of deep tendon reflex

(d) ascites.

Ix

(1) SGOT  $> 2$  Highly specific  
 SGPT for ALD.  
 (SGPT synthesis needs pyridoxine)

(1) SGOT  $\leq 1$ .  
 SGPT

(e) rGT - ↑

Site = Bile duct + ER

Fat squeeze ER to release rGT.

(g) rGT - ↑

(3) Peripheral Neutrophilia +

TNF $\alpha$  recruits

if neutrophil > 5500/mm<sup>3</sup>  
= Poor Prognosis

-

Rx:

① Fatty Liver = Reversible after cessation

FL = Reversible = Rx of underlying cause → obesity

② Hepatitis Doc-Steroid  
↓ act on TNF $\alpha$ .

Vit E.

↓ act as anti-oxidant

Indication if MADREY's  
alcoholic predominant funcn. > 32

$$= 4.6 \times [PT \text{ of pt} - PT \text{ of control}]_{(12 \text{ sec})} + S \cdot Bil$$

③ Cirrhosis

Best Rx → Liver Transplant

Cirrhosis

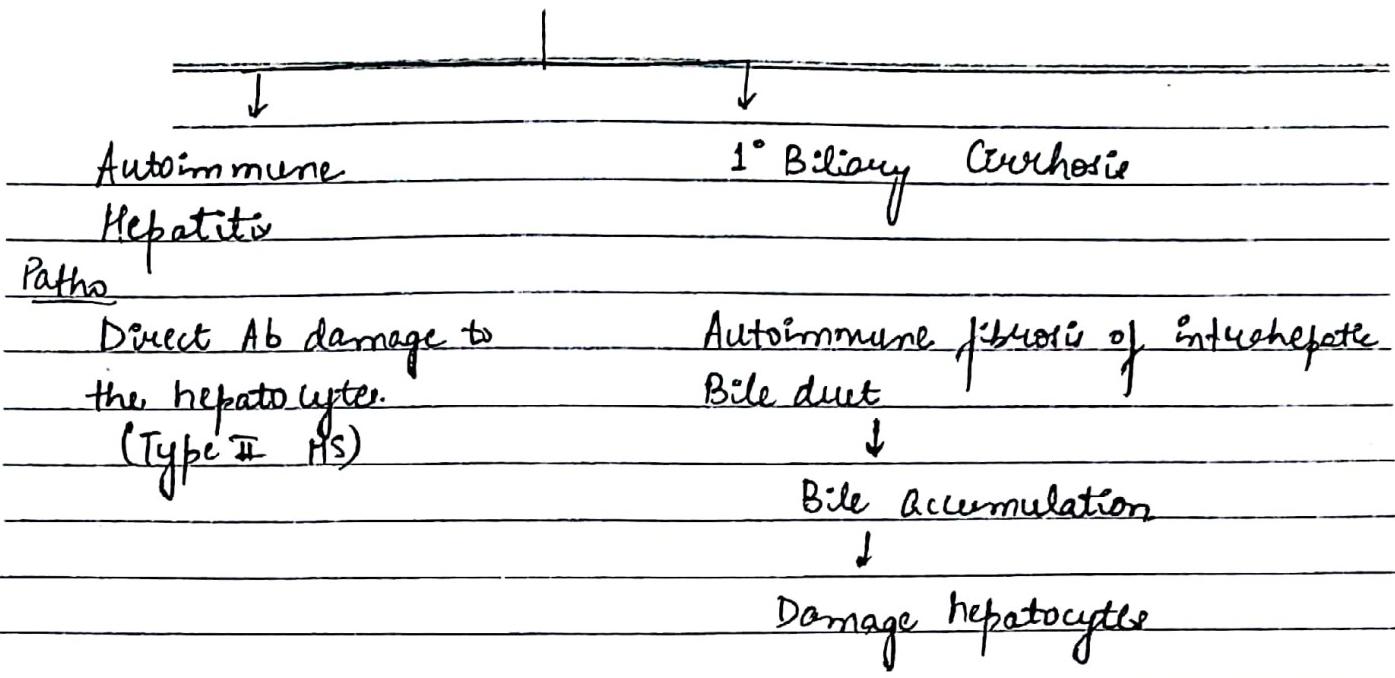
Liver Transplant

Recurrence of 1° disease

after LT = Nil of underlying cause Reman treated

# AUTOIMMUNE

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|                                      |           |                                                                 |
|--------------------------------------|-----------|-----------------------------------------------------------------|
| C/F                                  | ♀         | ♀                                                               |
| Age                                  | 20-40 yrs | 40-60 yrs                                                       |
| Recurrent<br>(months over years)     |           | Pruritus<br>Xanthelasma (cholesterol deficit in the eyelids)    |
| Inv Ab depends on type of<br>AIH M/c |           | Mc/Mast sensitive / Mast specific<br>Ab → Anti mitochondrial Ab |

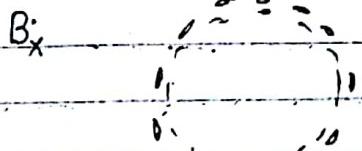
Inv Ab depends on type of  
AIH M/c

~~Ab~~  $\rightarrow$  (I) M/c  $\rightarrow$  (ANA) Most sensitive  
~~Ab~~  $\rightarrow$  Smooth muscle cell  
~~Ab~~  $\rightarrow$  P-ANCA

(II)  $\rightarrow$  Anti LKM1 (Liver kidney  
 $\downarrow$  microsome)  
 (also +ve in Hep C infection)

(III) - Least common, most severe  
 $\rightarrow$  Liver soluble antigen  
 Most specific

Regenerating hepatocytes

Bx: 

'Pseudo-rosette pattern'

Non-suppurative inflammation fibrosis  
of intrahepatic bile duct

R

① Hepatitis - Steroids (Doc)

① Compensated cirrhosis

Ursodeoxycholic Acid (UDCA)

(solubilize bile to non-toxic)

② Cirrhosis

Decompensated  $\rightarrow$  LT

② Decompensated cirrhosis

LT.

Recurrent after LT  $\rightarrow$

(common upto 50%)

Recurrence after LT  $\rightarrow$  flare

~~LMP Topic~~

## GENETIC

### WILSON'S DISEASE

Patho

AR mut<sup>n</sup> of  
ATP7B

$\downarrow$

$\downarrow$  Cu excretory protein  
in Liver

$\downarrow$   
Cu overload in the body

### HAEMOCHROMATOSIS

AR mut<sup>n</sup> of  
HFE

$\downarrow$

$\downarrow$  Hepcidin [ $\uparrow$  Fe absorption].

$\downarrow$   $\uparrow$  Fe absorption

Fe overload

qF

Liver

Most common  
organ

Liver

age < 20 yr

> 40 yr

Ch. Hepatitis +

+

|                                                                            |                                           |
|----------------------------------------------------------------------------|-------------------------------------------|
| Liver cirrhosis. Macronodular                                              | Mixed or Micronodular                     |
| HCC +                                                                      | ↑↑ (M/c cause of death even in t/td. ft.) |
| 2 <sup>nd</sup> organ affected CNS                                         | CNS                                       |
| ↳ Basal Ganglia                                                            | ↳ Hypothalamic pituitary axis             |
| M/c CNS manifestation                                                      | Hypogonadism                              |
| Frontal lobe                                                               |                                           |
| ↳ neuropsychiatric abnormalities.                                          |                                           |
| Cr. N/v → XII <sup>th</sup> (M/c Cr. N/v affected)<br>(Dysarthria)         |                                           |
| Autoimmune dysfunction.                                                    |                                           |
| ↳ Postural hypotension.                                                    |                                           |
| Not affected → 1. Sensory system<br>2. Motor power.<br>(Pyramidal pathway) |                                           |
| 3 <sup>rd</sup> Colour Change                                              |                                           |
| Eyes                                                                       | Skin.                                     |
| ↓ daytime vision = sunflower cataract                                      | due to Fe + melanin deposits<br>↓         |
| Kayser-Fleischer Ring (vision N)                                           | Bronze Pigmentation.                      |
| Peripheral                                                                 |                                           |

## (4) Functional Effect

Kidneys  
↓  
Proximal Tubular Dysfunction  
↓  
RTA - 2      Fancis Syndrome

Pancreas  
β cells affected  
↓

Bronze DM.

\* Reversible effect of haemochromatosis unlike other

## (5) Structural Damage

RBC Membrane  
↓  
Haemolytic Anaemia

Joints (2d 3rd MCP jt)  
Fe in joints → Pyrophosphate

Ca Pyrophosphate ↑

Pseudogout

(6)

X

CVS - Fe infiltrate inside myocyte

Myocyte contraction ↓



DCMP > RCMP

M/c cause of death ⇒ CVS in untreated pt.

Myocyte relaxation ↓



Inv

(N) Free Cu + Apoceruloplasmin  
↓  
Ceruloplasmin (Bound Cu)

|                                                        |                                                                       |
|--------------------------------------------------------|-----------------------------------------------------------------------|
| <u>Ab(N)</u> ↓ binding of free Cu to apo ceruloplasmin | 1. S. Fe → ↑<br>2. % Transferrin → ↑<br>Saturation                    |
| 1. S. Free Cu → ↑                                      | 3. S. Ferritin ↑                                                      |
| 2. S. Ceruloplasmin → ↓                                | 4. TIBC ↓<br><sup>New</sup> 5. UIBC ↓ = TIBC - S. Fe<br>(unsaturated) |
| 3. S. Total Cu = ↓<br>(mainly in bound form)           | ↑ Most sensitive inv                                                  |
| 4. Urinary free Cu levels - ↑                          | 6. Bx → ↑ Fe.<br>Prussian Blue Stain                                  |
| 5. Bx - Liver Cu > 200 µg/g<br>dry liver wt.           |                                                                       |

|                 |                                                          |
|-----------------|----------------------------------------------------------|
| <u>R</u>        | Hepatitis → Zn (DOC) [50mg/d]                            |
|                 | ↓                                                        |
| ① Cu absorption | Hepatitis →<br>DOC → Phlebotomy                          |
|                 | • 1mL Blood will remove → 0.5mg Fe                       |
|                 | • Single phlebotomy → 500mL Blood.<br>(250mg Fe removed) |
|                 | • Fe overload. > 20g                                     |
|                 | 80 phlebotomy Req.                                       |

|                                                 |                                  |
|-------------------------------------------------|----------------------------------|
| 2) Cirrhosis -                                  | Cirrhosis → Liver Transplant     |
| According to NAZER SCORE                        | Recurrence after LT → rare < 10% |
| • SGOT                                          |                                  |
| • S. Bil                                        |                                  |
| • PT.                                           |                                  |
| ↓                                               |                                  |
| <7      7-9      >9                             |                                  |
| Zinc + LT                                       |                                  |
| Treatment pt. will be lifelong                  |                                  |
| Recurrence after LT → NIL <sup>Zn</sup> therapy |                                  |

Q.  $\text{C}^+$  causes  $\uparrow \text{Cu}$  in Liver = KF Meng -

- a) autoimmune cholangitis
- b) 1° Biliary cirrhosis
- c) 1° sclerosing cholangitis
- d) All

} Ch4. cholestatic conditions

Q. After Phlebotomy manifestation of haemochromatosis ?

Reversible

- Hepatomegaly
- Skin pigmentation
- Diabetes
- CHF

Irreversible

- Cererosis
- Arthritis
- Hypogonadism

Q. HFE mutation  $\uparrow$  risk of  $\text{C}^+$  cancer = Breast  
colon cancer

## COMPLICATIONS OF LIVER FAILURE

### 1) HEPATIC ENCEPHALOPATHY

Mech- ↓ urea cycle



$\uparrow \text{NH}_3$

Astrocyte Damage

C/F- West HAYEY's Grading

|            |     |                                                                                                    |
|------------|-----|----------------------------------------------------------------------------------------------------|
| Restless   | I   | Earliest symptom = altered sleep cycle<br>" sign = altered handwriting<br>(constructional aphaxia) |
| Drowsiness | II  |                                                                                                    |
| Stuporosus | III | Trail making test<br>join to ① to ② 5 numbered circles.                                            |
| Coma       | IV  | (Normal time 15-30s.)                                                                              |

|                             |   |  |
|-----------------------------|---|--|
| Deep coma                   | V |  |
| <u>Inv</u>                  |   |  |
| EEG → ① most characteristic |   |  |

Triphasic large amplitude wave (grade II to IV)

② Slow - Grade V (1-4 Hz)

|                                                   |                                                                 |                                               |
|---------------------------------------------------|-----------------------------------------------------------------|-----------------------------------------------|
| Rx                                                |                                                                 |                                               |
| ▷ Rx [ppt cause]                                  | Mech.                                                           | Rx                                            |
| ① GI infection                                    | ↑ bacterial proliferation                                       | Ab of choice<br>Atc Rifaximin.<br>(550 mg BD) |
| ② upper GI bleed<br>(ruptured esophageal varices) | Blood protein<br>↓ reach<br>gut bacteria<br>↳ ↑ NH <sub>3</sub> | If vital stable → Ryle's tube aspiration.     |

Rx OC → Endoscopic Band  
Ligation of Varices

Doc → Octreotide

2° prophylaxis -  $\beta$  blockers  
(never in acute bleed)

⑤  $S \cdot K^+ \downarrow$

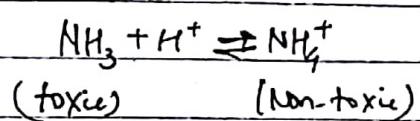
## L Peristaltis

## I.V. KCl infusion

10-20 mm/ hour.

## Bacterial Profigeration

## ④ Metabolic alkalosis



Rx underlying cause

vomiting  
(Ice cream)

if pH ↓ → eq. shifts to (R)

## ⑤ Constipation

## Bacterial proliferation

Laxative of choice 2

## Lactulose

Cause added p.H.

1

Target 2-3 stools/day  
Otherwise may cause diarrhea

## (6) Myxovolemie

$\uparrow$  Renin  $\rightarrow$   $\uparrow$  aldosterone

GT → BL

1

$S \cdot K^+ / \text{at}$

## Lactate

## Met. alklosis

HCO<sub>3</sub><sup>-</sup>

## Metabolism

So, I.V. fluid → NS

## ⇒ ASCITES

\* Mech. ↑ Sinusoidal pressure (compression by nodules)

+

Na & H<sub>2</sub>O retention ←

↑ NO synthase (NO degraded in Liver)

↓

Aldosterone ↑

↑ NDO

Systemic vasodilation

(Blood pooling in  
systemic circulation)

Pulmonary  
vasodilation

Renin ↑

↑

↓ Renal perfusion ↓

Hepato-Renal  
Syndrome

\* C/F.

Sign  
Mast PUDDLE

Min fluid needed  
120 mL

Shifting dullness

← 500 mL

Fluid thrill

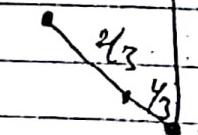
← 1500 mL

\* Inv Ascitic fluid

- Preferred Site → (1) lower quadrant

- Needle Size = Diagnostic 20-22G  
Therapeutic 15G

Umbilicus



## Step ① S-albumin - Ascitic Albumen (SAAC<sub>1</sub>)

$< 1.1$

(⑩ Sinusoidal pressure)

- 1) If S-albumin  $\downarrow$   
eg. Nephrotic Syndrome

- 2) If Ascitic albumin  $\uparrow$

due to  $\uparrow$  Peritoneal venel  
permeability

$> 1.1$

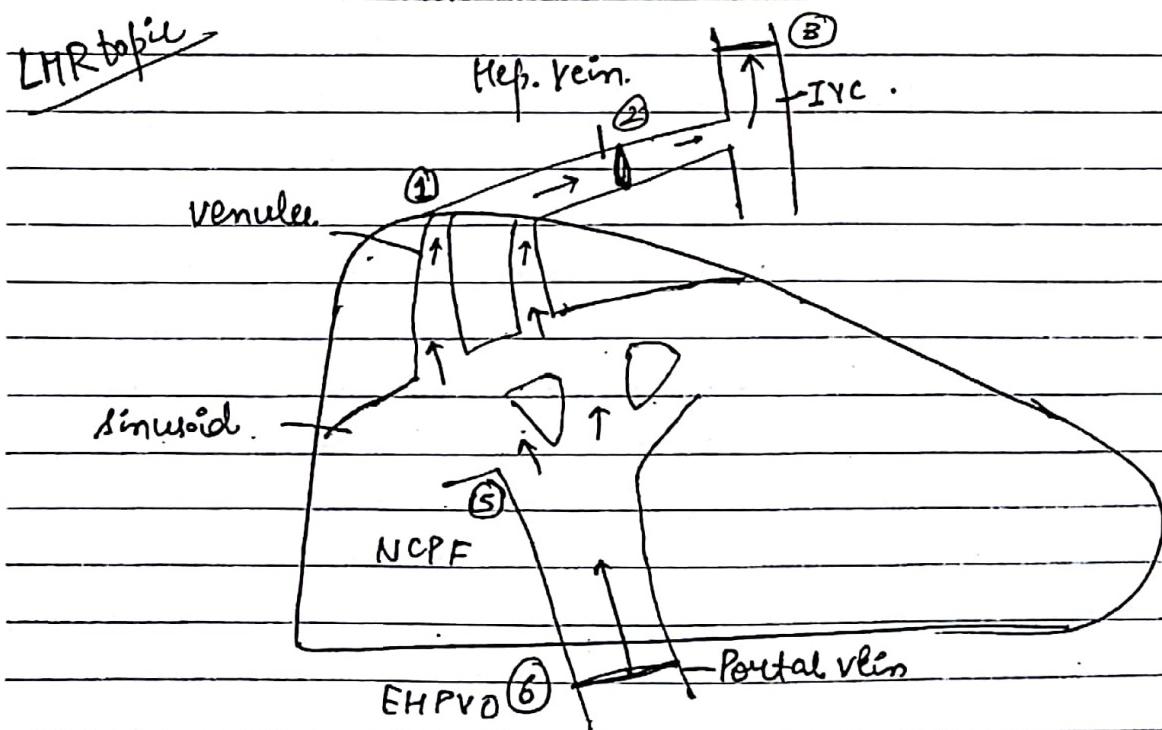
$\uparrow$  Sinusoidal pressure

- 1)  $\uparrow$  Ascitic albumen  $\downarrow$   
  - $\uparrow$  Sinusoidal pressure.
  - Sinusoidal wall is impermeable  
to albumin leak.

Eg. TB peritonci  
cancer

Acute Pancreatitis

Heart (9)



Step 2 - Ascitic Total Protein  $\leftarrow$  if  $SATT > 1.1$ ,

Cirrhosis

$< 2.5$

Non-cirrhotic

(Post-splenectomy ascites<sup>a</sup>)

$> 2.5$

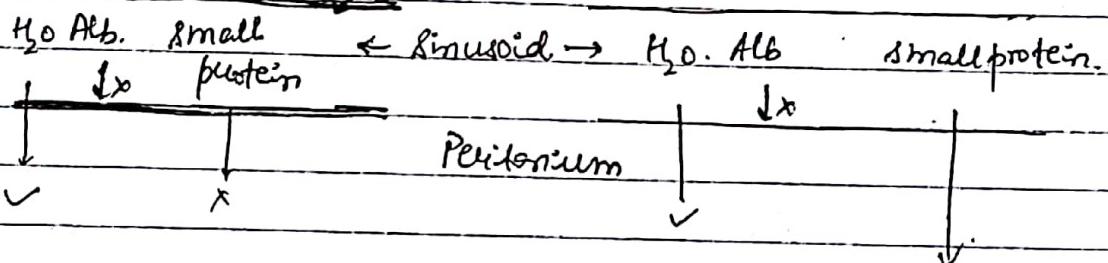
① Ven-occlusive Disease

② Budd-Chiari

③ IVC obstruction

④ CHF / Constrictive Pericarditis

Fibrosis



Rx

Grade

Defn

Rx

I = Mild Ascites

No clinical signs

salt restriction

II = Moderate

Clinical signs +ve

Add diuretics

Respiratory distress -

spirostolactone

(max - 400mg/day)

Furosemide

(max - 160 mg/d)

III. Severe

Resp. Distress +

Large vol. paracentesis  
(5-6L removed)

+

I.V. albumin

(to retain in fluid)

IV Refractory Ascites      No response  
 >7 days of Max dose of Both diuretics      Same as Grade III

(5) Non-Cirrhotic Portal Fibrosis

Age >20 yr

c/f upper GI bleed +  
 ↑

Portal HTN +  
 ↓

Spleen +  
 >7 cm below Costal margin

Jaundice (-)

Encephalopathy (-)

Ascites (-)

Rx - Endoscopic Band ligation +

(6) Extra-hepatic Porta Vein Occlusion

<20 yr.

+

+

+

<7 cm below costal margin

(-)

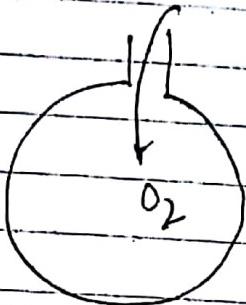
(-)

(-)

+

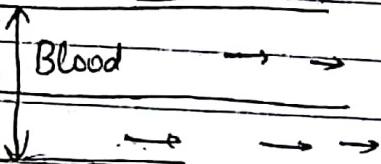
### 3. HEPATO - PULMONARY SYNDROME.

Mech. Pulmonary vasodilation



(N) Pulmonary artery diameter

If vasodil = diam  
occur increase



mixing of deoxygenated blood  
on L side

R to L shunt

C/F

Platypnoea - dyspnea ↑ on standing [ diaphragm moves down ]

shunt open

hypoxia ↑ ]

Inv

① ↓ in O<sub>2</sub> saturation by 3% on standing from supine  
Orthodeoxia

Rx → Sclerosis of dilated vessel

2) RxOc = Liver Transplant

# INTESTINAL

## MALABSORPTION DISEASES

due to SI disease

| Proximal       | Distal                    |
|----------------|---------------------------|
| ↑              | ↑                         |
| Fe, FA, Ca, Mg | Bile, Vit B <sub>12</sub> |
| Fat, CHO, ++   | +                         |
| Protein        |                           |

## Tests for malabsorption

### I) For Fat :-

- Gold Std → 72 hour stool fat estimation  
if fat excretion > 6% ⇒ Steatorrhoea



H/C abnormality seen in Malabsorption syndrome

### ② Spot I<sub>x</sub> → Sudan III stain.

+ve if stool fat > 10%

### II) For Carbohydrate :-

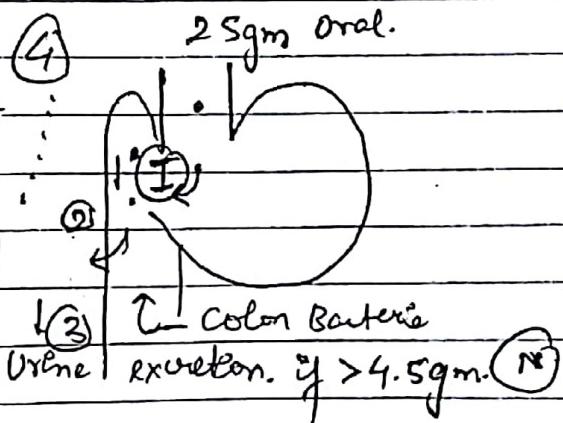
- Most specific I<sub>x</sub> → D Xylose Test

Cause of <4.5gm excretion Blood

1) Pyloric stenosis

2) Proximal

SI disease



3) Coeliac disease

4) Bacterial overgrowth syndrome

5) 3rd space loss → ascites

Pleural effusion.

(ii) Renal failure

(iii) Vit B<sub>12</sub> malabsorption  
SCHILLING's TEST

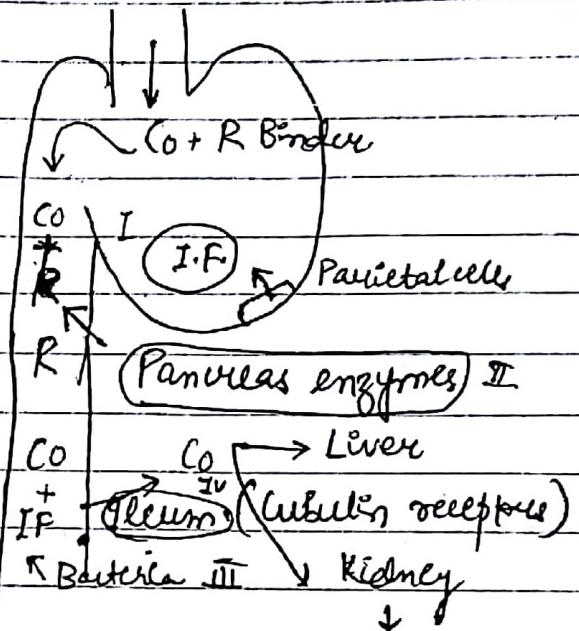
(i) Oral radiolabelled Cobalamine

+  
I.M. vit B<sub>12</sub> (1mg)  
to fill liver

↓  
24 hour Urine collection.

↓  
<10%  
↓  
malabsorption  
↓  
>10% of excretion  
↓  
(N) test

Cobalamine



1) I.F. → Pernicious Anaemia

2) Pancreatic enzyme → Ch. Pancreatitis

3) Ab x 5 days → Bacterial overgrowth syndrome

if remains < 10% → Ileum disease

Q. In dietary deficiency of B<sub>12</sub>, schilling test. (N)

Q. Mut' of cubulin (R)  $\rightarrow$  IMERSLUND CRIESBECK's SYNDROME

#### IV Intestinal Biopsy

Gold Std. Ix or Most Specific Ix for malabsorption.

#### Etiologies of Malabsorption -

| CELIAC SPRUE                                                                                          | TROPICAL SPRUE                                                   |
|-------------------------------------------------------------------------------------------------------|------------------------------------------------------------------|
| Cause GLIADIN Hypersensitivity<br>(+ve in gluten)<br>↓<br>Local Contact MS                            | Bacterial Toxin.<br>+<br>Folic acid deficiency (+mucosal repair) |
| Prox SI > Distal SI                                                                                   | Distal SI > Prox SI.                                             |
| Q/F * Age - Typical 6-12 months<br>can occur at any age<br>Spontaneous remission - 2nd decade         | Adults                                                           |
| * Steatorrhoea (large vol, foul smelling)<br>leading to ↓<br>Chronic >4 weeks.                        | ✓                                                                |
| Non-inflammatory<br>(No blood or pus in stool)                                                        |                                                                  |
| * Extra-intestinal manifestations.<br>H/c - Dermatitis Herpetiformis<br>Other - T, DM, IgA deficiency |                                                                  |

## COELIAC SPRUE

## TROPICAL SPRUE

Inv

① Serology +

Most specific Ab = Anti-Endomysial Ab.

Most sensitive Ab = Anti tissue

Transglutaminase (TTG)

Most sensitive + specific Ab / Mc Best  
= Anti TTG

② Biopsy

- Lon of villi + ] renewable after
- Flat mucosa + gluten free
- Lymphocyte infiltration + diet

+

+

+

③ HLA DQ2 (+) in 100% cases.

HLA DQ8 but non-specific

-

R

LX Gluten free diet

Antibiotics → Doxycycline or

Rifaximin.

+

Folic acid.

Duration of Hf → 6 months

2. Steroid. Indications

1) Refractory sprue

2) (no response upto 12 month)

of gluten free diet

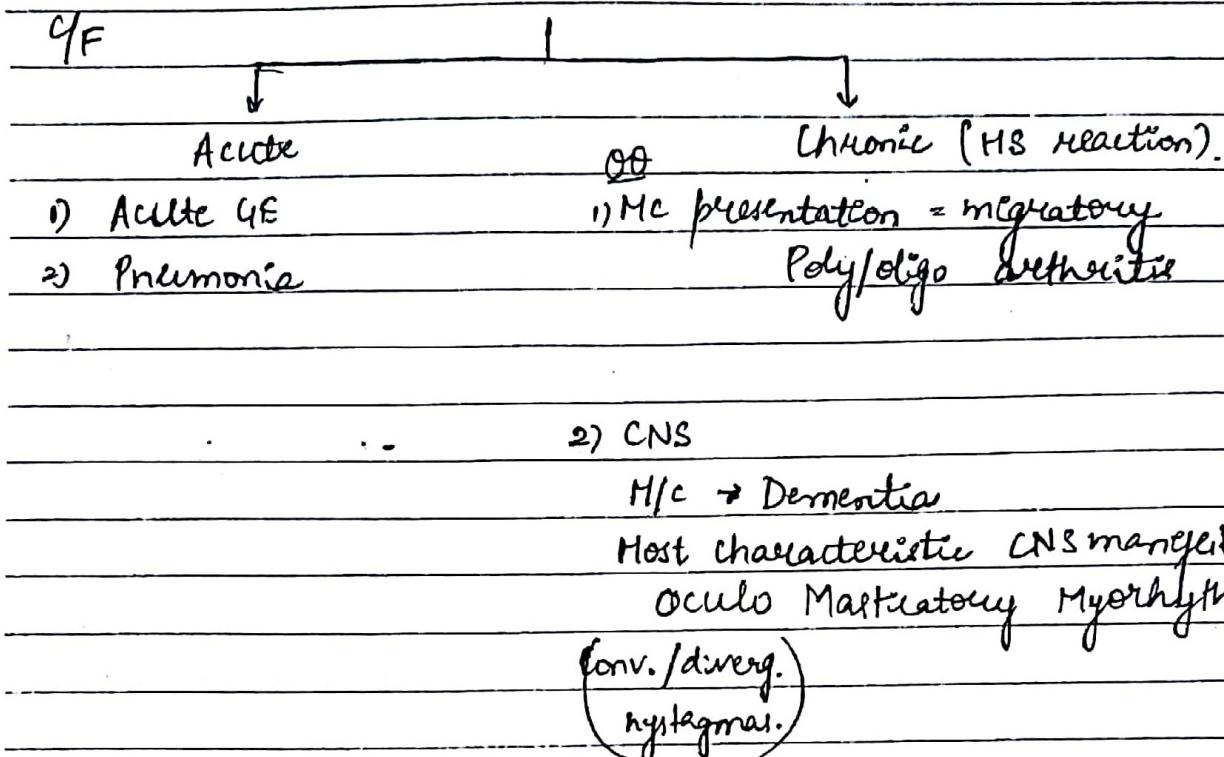
2) Celiac shock (↑ gluten load)

3) SI lymphoma

H/c cause of death

## WHIPPLE'S DISEASE

~~Also cause - Tropheryma Whipplei~~



### Other CNS manifestations

- Cerebellar ataxia
  - Myoclonic seizure
  - Encephalopathy
  - P. Neuropathy
  - ① organ not involved in whipple's
  - ② kidney
  - ③ lung
  - ④ eye
  - ⑤ CNS
- 3) CVS - Pericarditis
- M/c - Pericarditis

4) Eye - Uveitis

5) Polyserositis = Ascites  
Pleuritis

Inv B<sub>x</sub> - PAS +ve macrophage containing

D/D → TB

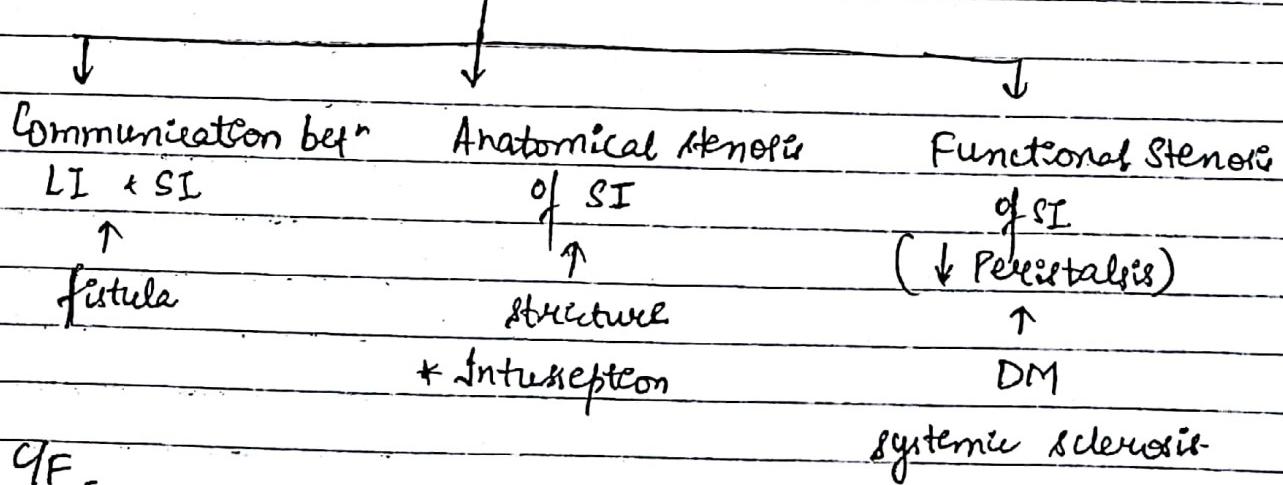
Bacilli  
AFB (-)

TB  
AFB (+)

Rx ① GIT → Ceftriaxone (2wk) → Cotrimoxazole (1yr)

② CNS/CVS → Ceftriaxone (2wk) → Doxycycline }  
(↑ risk of recurrence) + 1 year  
Chloroquine or Hydroxychloroquines }

BACTERIAL Overgrowth Syndrome  
Proliferation of colonic bacteria in prox SI  
Causes -



1) Steatorrhoea      Bile is deconjugated by bacteria in S.I.

Inr.

1) 72 hour stool test.  $>6\%$

2) D-Xylose test

excretion  $<4.5 \text{ gm}$

3) Schilling Test ab (N)

4) S-Folic acid level ↑

(Synthesis by bacteria + reabsorbed by prox. SI mucosa).

5) Lactulose Breath test or H<sup>2</sup> Breath test.



+ve in Breath 2-8 hours after giving Lactulose  
as Bacteria in SI metabolise.

6) Endoscopic jejunal aspirate culture



MIC organism E.coli  $>10^5/\text{mL}$

Rx

1) T/t underlying cause

2) Cyclo Ab. antibiotic [Co-amoxyclav.

Ab x 1 week



gap 3 wk.

↓  
Ab 1wk

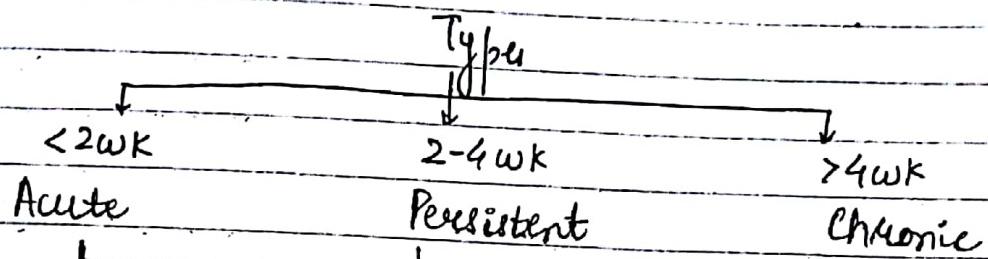
## APPROACH TO DIARRHOEA

Essential Criteria for Diarrhoea

Stool Vol.  $> 200 \text{ mg/d}$

Stool wt.  $> 200 \text{ mg/d}$

Duration.



90% Due to infections

Acute & Persistent

If Infectious Diarrhoea

$\geq 90\%$  due to non-infectious

Toxin induced

( $\uparrow$  electrolyte +  $H_2O$  secretion)

Inflammation induced  
(exudative)

- Fever  $\ominus$
- Pus in stool  $\ominus$
- Blood in stool  $\ominus$

$\oplus$

$\oplus$

$\oplus$

If Toxin induced

Preformed  
I.P.  $\tau$  in hours

Enterotoxin  
1-2 days

1) *Bacillus cereus*  
(Chinese Restaurant diarrhoea)

2) *Vibrio cholerae*  
( $\uparrow HCO_3$  in stool - Rice stool  
Watery stool)

2) *Staph. aureus.*

2) Enterotoxigenic *E.Coli*

M/CC of Traveller's diarrhoea

3) *Clostridium Perfringens*

If inflammation induced

I. Mild = mucosa limited. (blood in stool -)

II. M/c Viral diarrhoea in adults = Noro virus  
" " " children = Rota virus

II Mod. = submucosa

1) *Salmonella* → involves ileum  
↓

Bile reabsorp<sup>n</sup> ↓  
↓

Bile in stool.

III Severe

2) *Yersinia* → severe ileum inflammation  
Pseudo appendicitis

③ 3) *Campylobacter* J. M/c infection cause of GBS

III Severe = Deep layers

1) *Shigella* → Toxic encephalopathy  
Ekbli Syndrome

2) *E. histolytica* → flask shaped ulcer

Rx - acute/persistent diarrhea

(1) Essential - Rehydration

I.v. fluid of choice → RL contains

mmol/L  
K<sup>+</sup> 4

Na<sup>+</sup> 130

Ca<sup>2+</sup> 2

Cl<sup>-</sup> 109

Lactate 28

Osmolarity 273

slightly hyperosmolar

(2) Antibiotics

Indication - Mod to severe inflammatory infection diarrhea

If  $\geq 1$  of 3 criteria (+)

a) Fever  $> 101^{\circ}\text{F}$

b) Blood in stool

c) Pus in stool

Empirical = Fluroquinolone.

Chronic Diarrhea

Non-inflammatory  
e.g. Malabsorption  
Syndrome

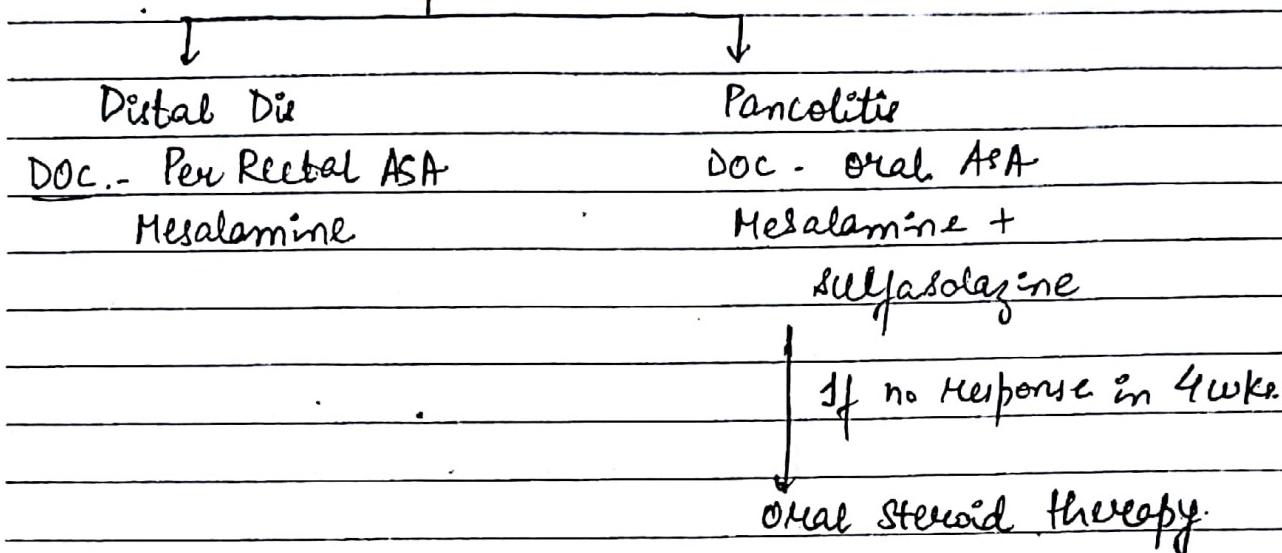
Inflammatory  
Topic LMR [Ulcerative colitis] IBD  
[Crohn's Disease]

| UC                                                    | CD                                                            |
|-------------------------------------------------------|---------------------------------------------------------------|
| * Risk / associated                                   |                                                               |
| ① Smoking ↓                                           | ↑                                                             |
| ② appendectomy ↓                                      | ↑                                                             |
| ③ Drugs<br>OCP ↔                                      | ↔                                                             |
| Methyldopa ↑                                          | ↔                                                             |
| Ab use in 1 year ↑                                    | ↔                                                             |
| ④ Infections ↔                                        | ↑ Mc = Mycobacterium<br>Para TB.                              |
|                                                       | Infection ↓ risk of CD -<br><i>H. Pylori</i>                  |
| ⑤ Turner's ↑                                          | ↑                                                             |
|                                                       | NOT DOWN SYNDROME                                             |
| ⑥ IL-10 Receptor<br>deficiency                        | ↑                                                             |
| ⑦ anti-inflammatory<br>Early onset IBD.               |                                                               |
| C/F Intestinal                                        |                                                               |
| M/c site → Rectum +<br>Sigmoid.<br>Rectum only        | M/c site → SI + LI > SI only.<br>M/c isolated site - Sigmoid. |
| M/c isolated site - Rectum<br>Site not involved → SI. | Rectum is usually spared                                      |

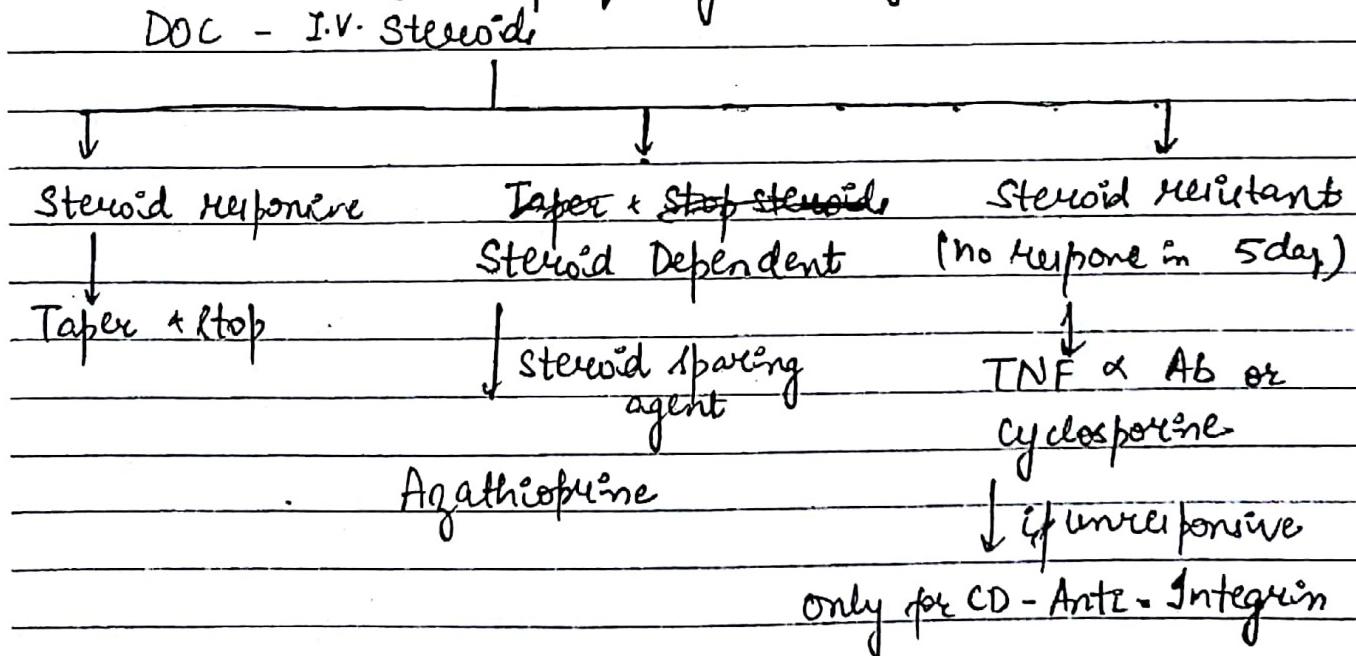
|                                                  |     |                                           |
|--------------------------------------------------|-----|-------------------------------------------|
| ① Malabsorption synd                             | (-) | (+)                                       |
| ② Bleeding PR (Tenesmus)                         | (+) | (-)                                       |
| ③ Fistula formation                              | (-) | (+) (Transmural involvement)              |
| ④ Toxic Megacolon.<br>(dilatation of colon >6cm) | (+) | (-) Bowel wall or thick stool dilatation  |
| Ulcer → Collar Button<br>○ (non-ulcering)        |     | Cobblestone ulcer<br># (eroding)          |
| Inv                                              |     |                                           |
| ① Stool exam.<br>Lactoferrin                     | (+) | (+)                                       |
| correlate w/ disease activity                    |     |                                           |
| Calprotectin                                     | (+) | (+)                                       |
| Predicts flare/re-lapse                          |     |                                           |
| ② Serology.<br>H/c → ANCA                        |     | Hc Ante<br>Saccharomyces cerevisiae<br>Ab |
| Role → ↑ risk of Pancolitis                      |     | Role → ↑ risk of early complication       |
| ③ Confirm $B_x$                                  |     | $B_x$                                     |

## Rx of Ulcerative Colitis

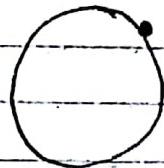
(I) Mild to mod. severity (stool freq. < 6/day)



II Severe IBD (Stool frequency > 6/day. or shock).



Only in Crohn's Disease (Resistant)



Integrin  $\beta_1$  helps in vascular adhesion

$\beta_1$

$\beta_7$  subunit

Lymphocyte

specific for GIT vessels

Ab against  $\beta_1$  &  $\beta_7$  = NATALIZUMAB.

(used in Multiple Sclerosis)

S/E → Reactivate JC virus

Progressive multifocal leukoencephalopathy

Ab against  $\beta_7$  = VEDOLIZUMAB

## Rx of Crohn's Disease

I. Mild to Mod. IBD



Stool limited

Doc - Oral release

Budesonide



Small + Large intestine

Doc - Oral prednisolone



no response in 4 weeks

Methotrexate

### \* Miscellaneous Points :-

1) Major cause of death → Cancer.

2) Colonic cancer risk → Ulcerative Colitis = Crohn's Disease.

3) Colonie Ca milk  $\downarrow \rightarrow$  Folic acid, ASA agents.

4) Extraintestinal Manifestation of IBD (usually more in CD)

Correlated to Bowel activity

Independent of Bowel activity

Skin - (1) Erythema Nodosum  
(red, hot, tender, nodules on skin)

N - neutrophil infiltration  
N - non-infective  
N - necrosis of skin.  
(2) Pyoderma Gangrenosum

Joints - Migratory Polyarthritis  
(Peripheral joints)

Ankylosing Spondylitis

Eye - Episcleritis

Uveitis

Liver - Non-alcoholic fatty  
Liver Disease

~~Set 1° R~~ Sclerosing Cholangitis

Risk factor for  
Cholangiocarcinoma

Q. M/c extra-intestinal organ affected in IBD - Joints

Q. M/c " " " manifestation.  $\rightarrow$  Erythema Nodosum

Q. C " " " more in UC  $\rightarrow$  Pyoderma  
1° sclerosing cholangitis

Addition Harrison Selected.

Part I → Involuntary wt. loss - Def<sup>n</sup> Cancer

Inv (Table)

Ascites

Table of causes of diarrhoea

Part II - Table of T/t of Hepatitis  
(Exclude doses or regimen)

Table of intestinal Biopsy findings

Protein losing enteropathy  
(1st 2 para - causes  
Inv)